PHILIP MORRIS U.S.A.

INTEROFFICE CORRESPONDENCE

Richmond, Virginia

To: Robin Kinser **Date:** July 10, 2002

From: Kathy Mitchell

Subject: Acrolein Biomarker: 3-hydroxypropylmercapturic acid

Files Searched:	Registry File	1957 - 7/2002
	CA File	1947 - 7/2002
	Biosis	1969 – 7/2002
	Medline	1958 – 7/2002

The registry number for the 3-hydroxypropylmercapturic acid was located. The table below summarizes the original name that you supplied, Chemical Abstracts name and Registry number, and synonyms used by authors. The registry records are attached.

Table 1. Names, Synonyms, and Registry Numbers for 3-hydroxypropylmercapturic acid

Supplied Name	3-hydroxypropylmercapturic acid
Chemical Abstracts Registry Number	23127-40-4
Synonyms	L-Cysteine, N-acetyl-S-(3-hydroxypropyl)- (CA Index Name) Alanine, N-acetyl-3-[(3-hydroxypropyl)thio]-, L- N-Acetyl-S-(3-hydroxypropyl)cysteine S-(3-Hydroxypropyl)mercapturic acid 3-OHPrMCA

Levels in Smokers vs. Non-smokers
A search in the Chemical Abstracts, Biosis and Medline literature files using the registry number was conducted and a set of 38 records was retrieved. All records were displayed and are attached. Only two records reported 3-hydroxypropylmercapturic acid as a metabolite of cigarette smoking. Urban et. al. presented "Urinary excretion of S-alkyl mercapturic acids as biomarkers for the exposure to electrophilic precursors in tobacco smoke " at 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology in 2001 (See page 6 below.).. Stanek et. al. investigated the use of tandem mass spectrometry for the determination of 3-hydroxypropylmercapturic acid and reported the results of the analysis the urine of one smoker and eight non-smokers (See page 27 below.).

No information on half-life was located.

Confounding exposures
Many researchers administered allyl compounds (esters, alcohols, halides) and haloalkanes to rats and mice which were metabolized to acrolein and were biotransformed and detected as 3-HPMA in urine or tissues (See pages 16, 18, 21, 31, 32, 34, 35, 36, 38, 39, 40, 46, 47, 48, 50 below).

The chemotherapy drug, cyclophosphamide, is metabolized to acrolein and 3-HPMA has been reported in urine by many investigators (See pages 23, 25, 31, 33, 41, 44, and 45 below.).

3-hydroxypropylmercapturic acid is reported as a metabolite of 1-3, butadiene (See pages 8, 10, and 19 below.).

A copy of the bibliographic information for each item is attached. Copies of the complete papers can be ordered in the library.

CHEMCIAL ABSTRACTS/BIOSIS/MEDLINE FILE SEARCH STRATEGY

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=> d que
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  23127-40-4/RN
L27     33 SEA FILE=CA ABB=ON  PLU=ON  L26
L28     10 SEA FILE=BIOSIS ABB=ON  PLU=ON  L26
L29      6 SEA FILE=MEDLINE ABB=ON  PLU=ON  L26
L30     38 DUP REMOVE L27 L28 L29 (11 DUPLICATES REMOVED)
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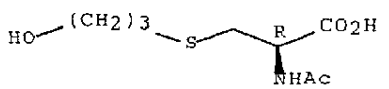
Kathy Mitchell

Attachment

Chemical Abstracts Registry File Record

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **23127-40-4** REGISTRY
CN L-Cysteine, N-acetyl-S-(3-hydroxypropyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, N-acetyl-3-[(3-hydroxypropyl)thio]-, L- (8CI)
OTHER NAMES:
CN 3-(Hydroxypropyl)mercapturic acid
CN N-Acetyl-S-(3-hydroxypropyl)cysteine
CN S-(3-Hydroxypropyl)mercapturic acid
FS STEREOSEARCH
DR 23127-19-7
MF C8 H15 N O4 S
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CSNB, MEDLINE,
TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

32 REFERENCES IN FILE CA (1967 TO DATE)
32 REFERENCES IN FILE CAPLUS (1967 TO DATE)

3-hydroxypropylmercapturic acid
(all records for the registry numbers from the Chemical Abstracts, Biosis, or Medline Bibilographic files)

L30 ANSWER 1 OF 38 CA COPYRIGHT 2002 ACS
AN 136:132166 CA Full-text
TI Mercapturic acids (N-acetylcysteine S-conjugates) as endogenous substrates for the renal organic anion transporter-1
AU Pombrio, James M.; Giangreco, Adam; Li, Liqiong; Wempe, Michael F.; Anders, M. W.; Sweet, Douglas H.; Pritchard, John B.; Ballatori, Nazzareno
CS Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA
SO Molecular Pharmacology (2001), 60(5), 1091-1099
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB Mercapturic acids are N-acetyl-L-cysteine S-conjugates that are formed from a range of endogenous and exogenous chems. Although the kidney is a major site for elimination of mercapturic acids, the transport mechanisms involved have not been identified. The present study examined whether mercapturic acids are substrates for the renal basolateral organic anion transporter-1 (Oat1) from rat kidney. This carrier mediates uptake of organic anions from the bloodstream in exchange for intracellular α-ketoglutarate. Uptake of [3H]p-aminohippuric acid (PAH) in Oat1-expressing Xenopus laevis oocytes was strongly inhibited by S-(2,4-dinitrophenyl)-N-acetyl-L-cysteine (DNP-NAC) and by all other mercapturic acids tested, including the endogenous mercapturic acid N-acetyl-leukotriene E4. Inhibition by the mercapturic acids was competitive, which is consistent with the hypothesis that these compds. are substrates for Oat1. This conclusion was supported by the direct demonstration of saturable [35S]DNP-NAC uptake in Oat1-expressing oocytes. [35S]DNP-NAC uptake was inhibited by PAH and other mercapturic acids and was stimulated in oocytes preloaded with glutarate. The apparent Km value for DNP-NAC uptake was only 2 μM, indicating that this mercapturic acid is a high affinity substrate for Oat1. Together, these data indicate that clearance of endogenous mercapturic acids is an important function of the renal organic anion transporter.
ST mercapturate conjugate substrate kidney org anion transporter 1
IT Cell membrane
(basolateral; mercapturic acids (N-acetylcysteine S-conjugates) as endogenous substrates for the renal organic anion transporter-1 (Oat1))
IT Biological transport
(carrier-mediated; mercapturic acids (N-acetylcysteine S-conjugates) as endogenous substrates for the renal organic anion transporter-1 (Oat1))
IT Kidney
(mercapturic acids (N-acetylcysteine S-conjugates) as endogenous substrates for the renal organic anion transporter-1 (Oat1))
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(organic anion-transporting, Oat1; mercapturic acids (N-acetylcysteine S-conjugates) as endogenous substrates for the renal organic anion transporter-1 (Oat1))
IT 57-66-9, Probenecid 616-91-1, N-Acetyl-L-cysteine 616-91-1D, N-Acetyl-L-cysteine, S-conjugates 2148-31-4 14402-54-1 15891-49-3, N-Acetyl-L-norleucine 19216-62-7 19542-77-9, N-Acetyl-S-benzyl-L-cysteine **23127-40-4** 23127-41-5 31386-36-4 35897-25-7, N-Acetyl-S-2,4-dinitrophenyl-L-cysteine 57596-70-0 80115-95-3,

N-Acetyl-leukotriene E4 89784-39-4 126637-66-9 173923-88-1
392333-36-7 392333-37-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mercapturic acids (N-acetylcysteine S-conjugates) as endogenous
substrates for the renal organic anion transporter-1 (Oat1))

IT 61-78-9, p-Aminohippuric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; mercapturic acids (N-acetylcysteine S-conjugates) as
endogenous substrates for the renal organic anion transporter-1 (Oat1))

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

L30 ANSWER 2 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:418592 BIOSIS Full-text
DN PREV200100418592
TI Urinary excretion of S-alkyl mercapturic acids as biomarkers for the exposure to electrophilic precursors in tobacco smoke.
AU Urban, M. (1); Meger, M. (1); Scherer, G. (1)
CS (1) Analytisch-biologisches Forschungslabor, Muenchen Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (2001) Vol. 363, No. 4 Supplement , pp. R167. print.
Meeting Info.: 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology Mainz, Germany March 13-15, 2001
ISSN: 0028-1298.
DT Conference
LA English
SL English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Biochemical Studies - General *10060
Metabolism - General Metabolism; Metabolic Pathways *13002
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Urinary System and External Secretions - Physiology and Biochemistry *15504
Toxicology - General; Methods and Experimental *22501
BC Hominidae 86215
IT Major Concepts
Metabolism; Toxicology
IT Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics; urine: excretory system
IT Chemicals & Biochemicals
S-(2-hydroxy)ethyl mercapturic acid [HEMA]: biomarker, plasma, urinary excretion; S-(3-hydroxy)propyl mercapturic acid [HPMA]: biomarker, plasma, urinary excretion; S-cyanoethyl mercapturic acid [CEMA]: biomarker, plasma, urinary excretion; S-ethyl mercapturic acid [EMA]: biomarker, plasma, urinary excretion; S-methyl mercapturic acid [MMA]: biomarker, plasma, urinary excretion; acrolein: inhalation; cotinine: plasma, urinary; thioethers: formation, urinary
IT Miscellaneous Descriptors
cigarette: daily consumption; passive smoking; tobacco smoke; Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): non-smoker, smoker
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **23127-40-4** (S-(3-HYDROXY)PROPYL MERCAPTURIC ACID)
107-02-8 (ACROLEIN)
486-56-6 (COTININE)

L30 ANSWER 3 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 1
AN 134:175222 CA Full-text
TI High-performance liquid chromatographic-tandem mass spectrometric determination of 3-hydroxypropylmercapturic acid in human urine
AU Mascher, D. G.; Mascher, H. J.; Scherer, G.; Schmid, E. R.
CS Ferdinand-Pichler-Gasse 2, Pharm Analyt Laboratory GmbH, Baden, A-2500, Austria
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 750(1), 163-169
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
CC 9-16 (Biochemical Methods)
AB A sensitive and specific HPLC-tandem mass spectrometric (HPLC-MS-MS) method was developed for the determination of 3-hydroxypropylmercapturic acid (3-HPMA) in human urine. Samples were extracted using ENV+ cartridges and then injected onto a C8 Superspher Select B column with MeCN and formic acid as eluent (5:95, volume/volume). N-Acetylcysteine was used as internal standard for HPLC-MS-MS. Linearity was given in the tested range of 50-5000 ng/mL urine. The limit of quantification was 50 ng/mL. Precision, as CV, in the tested range of 50-5000 ng/mL was 1.47-6.04%. Accuracy ranged from 87 to 114%. 3-HPMA was stable in human urine at 37° for 24 h. The method was able to quantify 3-HPMA in urine of nonsmokers and smokers.
ST HPLC tandem MS hydroxypropylmercapturate detn urine
IT HPLC
Tandem mass spectrometry
Urine analysis
(high-performance liquid chromatog.-tandem mass spectrometric determination of
3-hydroxypropylmercapturic acid in human urine)
IT **23127-40-4**, 3-Hydroxypropylmercapturic acid
RL: ANT (Analyte); ANST (Analytical study)
(high-performance liquid chromatog.-tandem mass spectrometric determination of
3-hydroxypropylmercapturic acid in human urine)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

L30 ANSWER 4 OF 38 CA COPYRIGHT 2002 ACS
AN 131:224695 CA Full-text
TI Quantitative and qualitative differences in the metabolism of 14C-1,3-butadiene in rats and mice: relevance to cancer susceptibility
AU Richardson, Kevan A.; Peters, Melanie M. C. G.; Wong, Brian A.; Megens, Rene H. J. J. J.; Van Elburg, Paul A.; Booth, Ewan D.; Boogaard, Pieter J.; Bond, James A.; Medinsky, Michele A.; Watson, William P.; Van Sittert, Nico J.
CS Shell International Chemicals, Toxicology Department, Shell Research and Technology Centre Amsterdam, Amsterdam, 1030 BN, Neth.
SO Toxicological Sciences (1999), 49(2), 186-201
CODEN: TOSCF2; ISSN: 1096-6080
PB Oxford University Press
DT Journal
LA English
CC 4-6 (Toxicology)
AB 1,3-Butadiene (butadiene) is a potent carcinogen in mice, but not in rats. Metabolic studies may provide an explanation of these species differences and their relevance to humans. Male Sprague-Dawley rats and B6C3F1 mice were exposed for 6 h to 200 ppm [2,3-14C]-butadiene (specific radioactivity [sa] 20 mCi/mmol) in a Cannon nose-only system. Radioactivity in urine, feces, exhaled volatiles and 14C-CO2 were measured during and up to 42 h after exposure. The total uptake of butadiene by rats and mice under these exptl. conditions was 0.19 and 0.38 mmol (equivalent to 3.8 and 7.5 mCi) per kg body weight, resp. In the rat, 40% of the recovered radioactivity was exhaled as 14C-CO2, 70% of which was trapped during the 6-h exposure period. In contrast, only 6% was exhaled as 14C-CO2 by mice, 3% during the 6-h exposure and 97% in the 42 h following cessation of exposure. The formation of 14C-CO2 from [2,3-14C]-labeled butadiene indicated a ready biodegradability of butadiene. Radioactivity excreted in urine accounted for 42% of the recovered radioactivity from rats and 71% from mice. Small amts. of radioactivity were recovered in feces, exhaled volatiles and carcasses. Although there was a large measure of commonality, the exposure to butadiene also led to the formation of different metabolites in rats and mice. These metabolites were not found after administration of [4-14C]-1,2-epoxy-3-butene to animals by i.p. injection. The results show that the species differences in the metabolism of butadiene are not simply confined to the quant. formation of epoxides, but also reflect a species-dependent selection of metabolic pathways. No metabolites other than those formed via an epoxide intermediate were identified in the urine of rats or mice after exposure to 14C-butadiene. These findings may have relevance for the prediction of butadiene toxicity and provide a basis for a revision of the existing physiol. based pharmacokinetic models.
ST butadiene metab cancer susceptibility
IT Carcinogens
Feces
Organ, animal
Species differences
Toxicokinetics
Urine
(quant. and qual. differences in metabolism of butadiene in rats and mice and relevance to cancer susceptibility)
IT 106-99-0, 1,3-Butadiene, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(quant. and qual. differences in metabolism of butadiene in rats and mice and relevance to cancer susceptibility)
IT 106-99-0D, 1,3-Butadiene, metabolites, biological studies 124-38-9, Carbon dioxide, biological studies **23127-40-4** 51868-61-2
144889-50-9 159092-65-6 174674-84-1 176914-98-0 219965-83-0
219965-84-1 219965-85-2 219965-86-3 219965-87-4 219965-88-5

219965-89-6 219965-90-9
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(quant. and qual. differences in metabolism of butadiene in rats and mice and relevance to cancer susceptibility)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD

L30 ANSWER 5 OF 38 CA COPYRIGHT 2002 ACS
AN 130:120754 CA Full-text
TI Identification of novel metabolites of butadiene monoepoxide in rats and mice
AU Richardson, Kevan A.; Peters, Melanie M. C. G.; Megens, Rene H. J. J. J.; van Elburg, Paul A.; Golding, Bernard T.; Boogaard, Peter J.; Watson, William P.; Van Sittert, Nico J.
CS Toxicology Department Shell Research and Technology Centre, Shell International Chemicals, Amsterdam, 1030 BN, Neth.
SO Chemical Research in Toxicology (1998), 11(12), 1543-1555
CODEN: CRTOEC; ISSN: 0893-228X
PB American Chemical Society
DT Journal
LA English
CC 4-6 (Toxicology)
AB Differences in the metabolism of 1,3-butadiene (Bd) in rats and mice may account for the observed species difference in carcinogenicity. Previous studies of the metabolic fate of Bd have identified epoxide formation as a key metabolic transformation which gives 1,2-epoxy-3-butene (BMO), although some evidence of aldehyde metabolites is reported. In this study, male Sprague-Dawley rats and male B6C3F1 mice received single doses of [4-14C]BMO at 1, 5, 20, and 50 mg/kg of body weight (0.014, 0.071, 0.286, and 0.714 mmol/kg of body weight). Anal. of urinary metabolites indicated that both species preferentially metabolize BMO by direct reaction with GSH when given by i.p. administration. The excretion of (R)-2-(N-acetyl-L-cystein-S-yl)-1-hydroxybut-3-ene (I), 1-(N-acetyl-L-cystein-S-yl)-2-(S)-hydroxybut-3-ene (II), 1-(N-acetyl-L-cystein-S-yl)-2-(R)-hydroxybut-3-ene (III), and (S)-2-(N-acetyl-L-cystein-S-yl)-1-hydroxybut-3-ene (IV)accounted for 48-64% of urinary radioactivity in rats and 46-54% in mice. The metabolites originating from the R-stereoisomer of BMO (III and IV) predominated over those arising from the S-stereoisomer (I and II) in both species. III was formed preferentially in mice and IV in rats. The corresponding mercaptoacetic acids, S-(1-hydroxybut-3-en-2- yl)mercaptoacetic acid and S-(2-hydroxybut-3-en-1-yl)mercaptoacetic acid, were identified only in mouse urine (.apprx.20% of the recovered radioactivity). 4-(N-Acetyl-L-cystein-S-yl)-1,2-dihydroxybutane a metabolite derived from hydrolysis of BMO, accounted for 10-17% of the radioactivity in rat and 6-10% in mouse urine. 4-(N-Acetyl-L-cystein-S- yl)-2-hydroxybutanoic acid, 3-(N-acetyl-L-cystein-S-yl)propan-1-ol, and 3-(N-acetyl-L-cystein-S-yl)propanoic acid, also derived from the hydrolysis of BMO, were only present in the rat. Metabolites of 1,2,3,4-diepoxybutane (DEB) were not detected after administration of BMO in rat or mouse urine. This study showed both quant. and qual. differences in the metabolism of BMO with varying doses and between species. The data aid in the safety evaluation of Bd and contribute to the interpretation of math. models developed for quant. risk assessment and extrapolation of animals to humans.
ST butadiene monoepoxide metab species
IT Adipose tissue
Adrenal gland
Blood
Bone marrow
Brain
Carcinogens
Feces
Heart
Kidney
Liver
Lung
Muscle
Organ, animal

Spleen
Testis
Urine
(novel metabolites of butadiene monoepoxide in relation to species)

IT 930-22-3, 1,2-Epoxy-3-butene
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(novel metabolites of butadiene monoepoxide in relation to species)

IT 930-22-3D, 1,2-Epoxy-3-butene, metabolites **23127-40-4** 51868-61-2 219965-87-4 219965-88-5 219965-89-6
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(novel metabolites of butadiene monoepoxide in relation to species)

IT 144889-50-9P 159092-65-6P 219965-83-0P 219965-84-1P 219965-85-2P 219965-86-3P
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(novel metabolites of butadiene monoepoxide in relation to species)

IT 98-59-9, Tosyl chloride 616-91-1, N-Acetyl-L-cysteine 62214-39-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel metabolites of butadiene monoepoxide in relation to species)

IT 17177-50-3P, 1,2-Dihydroxy-3,4-epoxybutane 133095-74-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel metabolites of butadiene monoepoxide in relation to species)

IT 219965-90-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel metabolites of butadiene monoepoxide in relation to species)

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

L30 ANSWER 6 OF 38 CA COPYRIGHT 2002 ACS
AN 130:153935 CA Full-text
TI Determination of mercapturic acids using 1,4-dihydroxynaphthalene, a new matrix for matrix-assisted UV laser desorption/ionization mass spectrometry
AU Eskinja, Mirela; Zollner, Peter; Schmid, Erich R.
CS Coca-Cola Ges.m.b.H., Vienna, A-1230, Austria
SO European Mass Spectrometry (1998), 4(3), 157-162
CODEN: EMSPFW; ISSN: 1356-1049
PB IM Publications
DT Journal
LA English
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 22
AB Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI TOF-MS) was applied for the characterization of six N-acetylcysteine derivs. (mercapturic acids) of synthetic origin. The measurement of mercapturic acids can provide important information for the bio-monitoring of exposure to electrophilic compds. Five isomers of dihydroxynaphthalene were evaluated as MALDI matrixes, and of them, 1,4-dihydroxynaphthalene was found to be very effective, most suitable, and thus, was used for further measurements. It has efficient absorbance at 337 nm, low background matrix ion signals and low matrix adduction. In the pos.-ion mode only very weak signals were detected. In the neg.-ion mode, the spectra exhibited deprotonated mol. ions [M - H]- of high abundance and no adduct peaks or fragment ions were observed, and this enabled reliable mol. mass determination of all six mercapturic acids. A detection limit of 1 pmol (signal-to-noise ratio = 3) applied to the target was achieved, which is distinctly more sensitive than other detection methods. In addition, the data obtained for intensities of the deprotonated mol. ion [M - H]- enabled the recording of the degradation kinetics of solns. with two distinct pH values during five days. Among six investigated compds., only one, 1,2-dihydroxy-4-(N- acetylcysteinyl)butane (DIOL), was found not to be stable in aqueous solution
ST mercapturic acid MALDI TOF mass spectroscopy dihydroxynaphthalene matrix; acetylcysteine deriv MALDI TOF mass spectroscopy dihydroxynaphthalene matrix
IT Laser ionization mass spectrometry
(photodesorption, matrix-assisted; MALDI TOF mass spectral anal. of mercapturic acids by using dihydroxynaphthalene as a new matrix)
IT Laser desorption mass spectrometry
(photoionization, matrix-assisted; MALDI TOF mass spectral anal. of mercapturic acids by using dihydroxynaphthalene as a new matrix)
IT 571-60-8, 1,4-Dihydroxynaphthalene
RL: NUU (Other use, unclassified); USES (Uses)
(MALDI TOF mass spectral anal. of mercapturic acids by using dihydroxynaphthalene as a new matrix)
IT 4775-80-8 16637-59-5 19216-62-7 **23127-40-4** 31386-36-4
RL: PRP (Properties)
(MALDI TOF mass spectral anal. of mercapturic acids by using dihydroxynaphthalene as a new matrix)
IT 144889-50-9
RL: PRP (Properties)
(unstable in aqueous solns.; MALDI TOF mass spectral anal. of mercapturic acids by using dihydroxynaphthalene as a new matrix)
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

L30 ANSWER 7 OF 38 CA COPYRIGHT 2002 ACS
AN 129:226782 CA Full-text
TI Metabolism and distribution of [2,3-14C]acrolein in Sprague-Dawley rats. II. Identification of urinary and fecal metabolites
AU Parent, Richard A.; Paust, Douglas E.; Schrimpf, Margaret K.; Talaat, Rasmy E.; Doane, Rebecca A.; Caravello, Halina E.; Lee, Sung J.; Sharp, Dale E.
CS Consultox, Limited, Damariscotta, ME, 04543-1239, USA
SO Toxicological Sciences (1998), 43(2), 110-120
CODEN: TOSCF2; ISSN: 1096-6080
PB Academic Press
DT Journal
LA English
CC 4-3 (Toxicology)
AB The metabolites of [2,3-14C]acrolein in the urine and feces of Sprague-Dawley rats were identified after either i.v. administration in saline at 2.5 mg/kg or oral administration by gavage as an aqueous solution as either single or multiple doses at 2.5 mg/kg or as a single dose of 15 mg/kg. Selected urine and feces samples were pooled by sex and collection interval and profiled by combinations of reverse-phase, anion-exchange, cation-exchange, and ion-exclusion high-performance liquid chromatog. (HPLC). Feces were also profiled by size-exclusion chromatog. Metabolites were identified by comparison with well-characterized stds. by HPLC and by mass spectrometry. The urinary metabolites were identified as oxalic acid, malonic acid, N-acetyl-S-2-carboxy-2-hydroxyethylcysteine, N-acetyl-S-3-hydroxypropylcysteine, N-acetyl-S-2-carboxyethylcysteine, and 3-hydroxypropionic acid. The fecal radioactivity from the oral dose groups was partitioned into methanol-soluble, water-soluble, and insol. radioactivity, some of which could be liberated by dilute acid hydrolysis. HPLC anal. of these exts. revealed no discrete metabolites. Size-exclusion chromatog. indicated a mol. weight range of 2,000 to 20,000 Da for the radioactivity, which was unaffected by hydrolysis at reflux with 6 M acid or base. This radioactivity was thought to be a homopolymer of acrolein, which was apparently formed in the gastrointestinal tract. The pathways of acrolein metabolism were epoxidn. followed by conjugation with glutathione, Michael addition of water followed by oxidative degradation, and glutathione addition to the double bond either following or preceding oxidation or reduction of the aldehyde. The glutathione adducts were further metabolized to the mercapturic acids. (c) 1998 Society of Toxicology.
ST acrolein metabolite feces urine
IT Feces
Urine
(acrolein metabolites in rat excretions)
IT Metabolism, animal
(urinary and fecal metabolites of acrolein in rats)
IT 107-02-8, Acrolein, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proposed pathways for metabolism of acrolein in rats)
IT 107-02-8D, Acrolein, metabolites
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(urinary and fecal metabolites of acrolein in rats)
IT 141-82-2, Malonic acid, biological studies 144-62-7, Oxalic acid, biological studies 503-66-2, 3-Hydroxypropionic acid **23127-40-4**, N-Acetyl-S-3-hydroxypropylcysteine 51868-61-2, N-Acetyl-S-2-carboxyethylcysteine 151419-71-5
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); OCCU (Occurrence)
(urinary metabolites of acrolein in rats)

L30 ANSWER 8 OF 38 CA COPYRIGHT 2002 ACS
AN 129:90213 CA Full-text
TI Effects of SS320A, a new cysteine derivative, on the change in the number of goblet cells induced by isoproterenol in rat tracheal epithelium
AU Takahashi, Koichi; Mizuno, Hiroyuki; Ohno, Hiromitsu; Kai, Hirofumi; Isohama, Yoichiro; Takahama, Kazuo; Nagaoka, Shigeru; Miyata, Takeshi
CS Central Research Laboratories, SS Pharmaceutical Co., Ltd., Narita, 286-8511, Japan
SO Japanese Journal of Pharmacology (1998), 77(1), 71-77
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal
LA English
CC 1-9 (Pharmacology)
AB The effects of SS-320A ((-)-(R)-2-amino-3-(3-hydroxypropylthio)propionic acid) on the change in the number of goblet cells induced by isoproterenol in rat tracheal epithelium were examined Four types of goblet cells were characterized in the tracheal epithelium according to their size and staining affinity with Alcian blue (AB)/periodic acid Schiff (PAS). The rats were given 0.05 mg isoproterenol/kg i.p. daily for 14 days. Increases in AB/PAS-pos. cells that were recognizable as goblet cells were noted in the tracheal epithelium. When SS-320A (10-100 mg/kg orally) or propranolol (1 mg/kg s.c.) was administered before each injection of isoproterenol, the increase in the number of goblet cells induced by isoproterenol was inhibited. There was no difference between male and female rats with regard to this inhibitory action. The expectorants ambroxol, bromhexine, L-cysteine Et ester, and S-carboxymethylcysteine (100 mg/kg orally) had no inhibitory effects on the isoproterenol-induced change in the number of goblet cells. Four metabolites (M1 - M4) of SS-320A tested in rats also failed to inhibit the change induced by isoproterenol. SS-320A itself may have a beneficial effect against mucus hypersecretion in chronic respiratory diseases.
ST SS320A trachea epithelium goblet cell isoproterenol
IT Trachea (anatomical)
(epithelium; SS-320A cysteine derivative and isoproterenol effects on goblet cell nos. in rat tracheal epithelium)
IT Trachea (anatomical)
(goblet cell; SS-320A cysteine derivative and isoproterenol effects on goblet cell nos. in rat tracheal epithelium)
IT 7683-59-2, Isoproterenol 13189-98-5, Ss320a **23127-40-4**
51868-61-2 201666-28-6 209665-22-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(SS-320A cysteine derivative and isoproterenol effects on goblet cell nos. in rat tracheal epithelium)

L30 ANSWER 9 OF 38 CA COPYRIGHT 2002 ACS
AN 127:136065 CA Full-text
TI Fragmentation of protonated thioether conjugates of acrolein using low collision energies
AU Oberth, Christa H.; Jones, A. Daniel
CS Facility for Advanced Instrumentation, University of California, Davis, CA, 95616, USA
SO Journal of the American Society for Mass Spectrometry (1997), 8(7), 727-736
CODEN: JAMSEF; ISSN: 1044-0305
PB Elsevier
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 22
AB The protonated mercapturic acid conjugate of acrolein, S-(3-oxopropyl)-N-acetyl-L-cysteine (I), undergoes facile retro-Michael loss of acrolein in the gas phase. To determine whether extensive loss of acrolein would impede structural characterization of acrolein-peptide adducts, fragmentation reactions of a series of conjugates, formed by 1,4-Michael addition of acrolein to peptides and cysteine derivs., were investigated at collision cell potentials up to -50 V using a triple quadrupole mass spectrometer. Differences in fragmentation dynamics suggest protonation at the sulfur of the N-acetylcysteine conjugate I facilitates retro-Michael elimination of acrolein with a low activation energy relative to other fragmentations. Analogous fragmentation was eliminated after borohydride reduction of the aldehyde to an alc. Retro-Michael fragmentation was not significant for acrolein conjugates of glutathione derivs., suggesting that proton sequestration occurs in peptides with multiple amide linkages even when the peptide does not contain a basic amino group. An unexpected outcome of these expts. was the observation of a facile gas-phase cleavage of peptides on the N-terminal side of S-(3-oxopropyl)cysteine residues. Such fragmentation behavior may prove useful for locating cysteine residues in peptides.
ST peptide acrolein conjugate mass spectral fragmentation; cysteine acrolein conjugate mass spectral fragmentation
IT Peptides, reactions
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(cysteine-containing; mass spectral fragmentation of protonated thioether conjugates of acrolein using low collision energies)
IT Mass spectra
(mass spectral fragmentation of protonated thioether conjugates of acrolein using low collision energies)
IT 70-18-8, Glutathione, reactions 616-91-1, N-Acetylcysteine
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(mass spectral fragmentation of protonated thioether conjugates of acrolein using low collision energies)
IT **23127-40-4P** 28542-76-9P, N-Acetylglutathione 73605-93-3P 124521-13-7P 140226-30-8P 192940-78-6P 192940-85-5P 192940-88-8P
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(mass spectral fragmentation of protonated thioether conjugates of acrolein using low collision energies)
IT 107-02-8, Acrolein, reactions 27025-41-8, Oxidized glutathione
RL: RCT (Reactant); RACT (Reactant or reagent)
(mass spectral fragmentation of protonated thioether conjugates of acrolein using low collision energies)

L30 ANSWER 10 OF 38 MEDLINE
AN 1998085636 MEDLINE Full-text
DN 98085636 PubMed ID: 9423578
TI Allylmercapturic acid as urinary biomarker of human exposure to allyl chloride.
AU de Rooij B M; Boogaard P J; Commandeur J N; van Sittert N J; Vermeulen N P
CS Leiden-Amsterdam Centre for Drug Research (LACDR), Department of Pharmacochemistry, Free University, The Netherlands.
SO OCCUPATIONAL AND ENVIRONMENTAL MEDICINE, (1997 Sep) 54 (9) 653-61.
Journal code: 9422759. ISSN: 1351-0711.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980113
AB OBJECTIVE: To evaluate the use of urinary mercapturic acids as a biomarker of human exposure to allyl chloride (3-chloropropene) (AC). During three regular shut down periods in a production factory for AC, both types of variables were measured in 136 workers involved in maintenance operations. METHODS: Potential airborne exposure to AC was measured by personal air monitoring in the breathing zone. In total 205 workshifts were evaluated. During 99 workshifts no respiratory protection equipment was used. Mercapturic acid metabolites were measured in urinary extracts by gas chromatography-mass spectrometry (GC-MS). RESULTS: During 86 work shifts when no respiratory protection was used the air concentrations of AC were below the Dutch eight hour time weighted average (8 h-TWA) occupational exposure limit (OEL) of AC (3 mg/m3), whereas in 13 workshifts the potential exposure, as measured by personal air monitoring, exceeded the OEL (3.3 to 17 mg/m3). With the aid of GC-MS, 3-hydroxypropylmercapturic acid (HPMA) was identified as a minor and allylmercapturic acid (ALMA) as a major metabolite of AC in urine samples from the maintenance workers exposed to AC. The concentrations of ALMA excreted were in a range from < 25 micrograms/l (detection limit) to 3550 micrograms/l. The increases in urinary ALMA concentrations during the workshifts correlated well with the 8h-TWA air concentrations of AC (r = 0.816, P = 0.0001, n = 39). Based on this correlation, for AC a biological exposure index (BEI) of 352 micrograms ALMA/g creatinine during an eight hour workshift is proposed. In some urine samples unexpectedly high concentrations of ALMA were found. Some of these could definitely be attributed to dermal exposure to AC. In other cases garlic consumption was identified as a confounding factor. CONCLUSION: The mercapturic acid ALMA was identified in urine of workers occupationally exposed to airborne AC and the increase in ALMA concentrations in urine during a workshift correlated well with the 8 h-TWA exposure to AC. Garlic consumption, but not smoking, is a potential confounding factor for this biomarker of human exposure to AC.
CT Check Tags: Human; Male
Acetylcysteine: AA, analogs & derivatives
*Acetylcysteine: UR, urine
Adult
*Air Pollutants, Occupational: UR, urine
*Allyl Compounds: UR, urine
Biological Markers: UR, urine
Creatinine: UR, urine
*Environmental Monitoring
Garlic: ME, metabolism
Middle Age
Plants, Medicinal

Regression Analysis
Smoking: ME, metabolism

RN 107-05-1 (allyl chloride); **23127-40-4 (S-(3-hydroxypropyl)cysteine N-acetate)**; 60-27-5 (Creatinine); 616-91-1 (Acetylcysteine)

CN 0 (Air Pollutants, Occupational); 0 (Allyl Compounds); 0 (Biological Markers)

L30 ANSWER 11 OF 38 CA COPYRIGHT 2002 ACS
AN 125:78930 CA Full-text
TI Biotransformation of allyl chloride in the rat. Influence of inducers on the urinary metabolic profile
AU De Rooij, Ben M.; Commandeur, Jan N. M.; Groot, Ed J.; Boogaard, Pieter J.; Vermeulen, Nico P. E.
CS Leiden-Amsterdam Cent. Drug Res., Free Univ., Amsterdam, 1081 HV, Neth.
SO Drug Metab. Dispos. (1996), 24(7), 765-772
CODEN: DMDSAI; ISSN: 0090-9556
DT Journal
LA English
CC 4-3 (Toxicology)
AB We investigated the biotransformation of allyl chloride (AC) in rats to select potential urinary biomarkers of exposure. For this purpose, we developed anal. methods to measure different selected urinary metabolites of AC. The earlier described urinary metabolites of AC [allyl mercapturic acid (ALMA) and 3-hydroxypropyl mercapturic acid (HPMA)], as well as two urinary metabolites of ECH [α-chlorohydrin (α-CH) and 3-chloro-2-hydroxypropyl mercapturic acid (CHPMA)], were determined in this study. After i.p. administration of AC, in doses ranging from 66 to 590 μmol/kg, control rats excreted 30±6.5% of the AC dose as ALMA. HPMA was a minor urinary metabolite of AC (<3% of the AC dose), and, for this metabolite, no clear dose-excretion relation was found. Two other minor urinary metabolites were also found as well, namely CHPMA and α-CH, suggesting the formation of ECH. CHPMA excretion was linear from 66 to 330 μmol/kg AC and amounted to 0.21±0.08% of the AC dose. α-CH excretion was linear in the dose range used and was excreted for 0.13±0.02% of the AC dose. In addition, we investigated the influence of three different enzyme inducers on the urinary metabolite profile of AC, namely pyrazole, β-naphthoflavone, and phenobarbital. Pyrazole only increased the urinary excretion of α-CH. β-Naphthoflavone induction only enhanced the ALMA excretion significantly. Phenobarbital induced both the excretion of CHPMA and α-CH. From these studies, we conclude that urinary excretion of ALMA, CHPMA, and α-CH can be used as biomarkers in humans potentially exposed to AC. However, ALMA seems to be the more appropriate biomarker, because enzyme induction may play a confounding role in CHPMA or α-CH is used.
ST allyl chloride metab urine metabolite
IT Urine
(allyl chloride metabolism in relation to urinary metabolic profile)
IT 107-05-1, Allyl chloride
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(allyl chloride metabolism in relation to urinary metabolic profile)
IT 96-24-2, α-Chlorohydrin 107-05-1D, Allyl chloride, metabolites **23127-40-4**, 3-Hydroxypropyl mercapturic acid 23127-41-5, Allyl mercapturic acid 97729-49-2, L-Cysteine, N-acetyl-S-(3-chloro-2-hydroxypropyl)-
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(allyl chloride metabolism in relation to urinary metabolic profile)

L30 ANSWER 12 OF 38 CA COPYRIGHT 2002 ACS
AN 124:335420 CA Full-text
TI Characterization of Urinary Metabolites from Sprague-Dawley Rats and B6C3F1 Mice Exposed to [1,2,3,4-13C]Butadiene
AU Nauhaus, Sara K.; Fennell, Timothy R.; Asgharian, Bahman; Bond, James A.; Sumner, Susan C. J.
CS Chemical Industry Institute of Toxicology, Research Triangle Park, NC, 27709, USA
SO Chem. Res. Toxicol. (1996), 9(4), 764-773
CODEN: CRTOEC; ISSN: 0893-228X
.DT Journal
LA English
CC 4-6 (Toxicology)
AB Male Sprague-Dawley rats and B6C3F1 mice were exposed to 800 ppm [1,2, 3,4-13C]butadiene for 5 h, and urine was collected during and for 20 h following exposure. Urinary metabolites were characterized using 1- and 2-dimensional methods of NMR spectroscopy. Three metabolites previously detected in vivo, N-acetyl-S-(2-hydroxy-3-butenyl)-L-cysteine, N-acetyl-S-(1-(hydroxymethyl)-2-propenyl)-L-cysteine, and N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine, were present in both rat and mouse urine, accounting for 87% and 73% of the total metabolites excreted, resp. A fourth metabolite, previously detected in vitro, 3-butene-1,2-diol, was also present in both rat and mouse urine and comprised 5% and 3% of the total metabolites excreted, resp. An addnl. metabolite detected only in mouse urine that is derived from glutathione conjugation with epoxybutene was identified as S-(1-(hydroxymethyl)-2- propenyl)-L-cysteine (4%). N-Acetyl-S-(1-hydroxy-3-butenyl)-L-cysteine (4%), detected in mouse urine, is a thiohemiacetal product of 3-butenal. Addnl., mice excreted N-acetyl-S-(3-hydroxypropyl)-L-cysteine (5%) and N-acetyl-S-(2-carboxyethyl)-L-cysteine (5%), which could be derived from further metabolism of N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine or from glutathione conjugation with acrolein. Mice excreted N-acetyl-S-(1- (hydroxymethyl)-3,4-dihydroxypropyl)-L-cysteine (5%), which could be derived from glutathione conjugation with diepoxybutane (BDE), while rats excreted 1,3-dihydroxypropanone (5%), which may be derived from hydrolysis of BDE. These studies indicate that reactive aldehydes are produced as metabolites of 1,3-butadiene (BD) in vivo, in addition to the reactive monoepoxide and diepoxide of BD. The greater toxicity of BD in mice compared with rats may be attributed to the greater ability of rats to detoxify BDE via hydrolysis, and/or to the production of reactive aldehydes.
ST urine metabolite butadiene species
IT Urine
(urinary metabolites of butadiene in relation to species)
IT 106-99-0, 1,3-Butadiene, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(urinary metabolites of butadiene in relation to species)
IT 96-26-4 106-99-0D, 1,3-Butadiene, metabolites 497-06-3, 3-Butene-1,2-diol **23127-40-4** 51868-61-2 144889-50-9 144889-51-0 159092-64-5 176914-96-8 176914-97-9 176914-98-0
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(urinary metabolites of butadiene in relation to species)

L30 ANSWER 13 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 2
AN 124:79076 CA Full-text
TI Biotransformation of acrolein in rat: excretion of mercapturic acids after inhalation and intraperitoneal injection
AU Linhart, I.; Frantik, E.; Vodickova, L.; Vosmanska, M.; Smejkal, J.; Mitera, J.
CS Centre Industrial Hygiene Occupational Diseases, National Inst. Public Health, Prague, CZ-100 42, Czech Rep.
SO Toxicol. Appl. Pharmacol. (1996), 136(1), 155-60
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
CC 4-3 (Toxicology)
AB Biotransformation of acrolein (ACR) was studied in vivo in the rat following inhalation and i.p. administration. The major and minor urinary metabolites were 3-hydroxypropylmercapturic acid (HPMA) and 2-carboxyethylmercapturic acid (CEMA), resp. Male Wistar rats were exposed to ACR, 23, 42, 77 and 126 mg/m3, for 1 h. The sum of mercapturic acids HPMA and CEMA excreted within 24 h after the exposure amounted to 0.87 ± 0.12, 1.34 ± 0.5, 2,81 ± 1.15, and 7.13 ± 1.56 μmol/kg, i.e. 10.9 ± 1.5, 13.3 ± 5.0, 16.7 ± 6.9, and 21.5 ± 4.8% of the evaporating absorbed dose, resp. The dose estimate was based on reported values of minute respiratory volume and respiratory tract retention and was corrected for the ACR-induced changes in minute respiratory volume In the relevant dose range (8.9 to 35.7, μmol/kg) the portion of mercapturic acids excreted was nearly constant for i.p. exposed rats. The sum of HPMA and CEMA amounted to 29.1 ± 6.5% of the dose. These results indicate that the deficiency in rat lung metabolism of ACR to acrylic acid previously observed is not compensated by the other detoxication pathway in vivo, mercapturic acid formation. The health hazard arising from inhalation of ACR is likely to be higher than that form other routes of exposure.
ST acrolein metab mercapturate urine
IT Urine
(acrolein metabolism and excretion of mercapturic acids after inhalation and i.p. injection)
IT 107-02-8, Acrolein, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(acrolein metabolism and excretion of mercapturic acids after inhalation and i.p. injection)
IT **23127-40-4**, 3-Hydroxypropylmercapturic acid 51868-61-2
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(acrolein metabolism and excretion of mercapturic acids after inhalation and i.p. injection)

L30 ANSWER 14 OF 38 CA COPYRIGHT 2002 ACS
AN 122:308479 CA Full-text
TI Identification of N-Acetylcysteine Conjugates of 1,2-Dibromo-3-chloropropane: Evidence for Cytochrome P450 and Glutathione Mediated Bioactivation Pathways
AU Weber, Gregory L.; Steenwyk, Rick C.; Nelson, Sidney D.; Pearson, Paul G.
CS Drug Metabolism Research, The Upjohn Company, Kalamazoo, MI, 49001, USA
SO Chem. Res. Toxicol. (1995), 8(4), 560-73
CODEN: CRTOEC; ISSN: 0893-228X
DT Journal
LA English
CC 4-6 (Toxicology)
Section cross-reference(s): 23
AB The haloalkane 1,2-dibromo-3-chloropropane (DBCP) is a carcinogen, mutagen, nephrotoxin, and testicular toxin. The identification of N-acetylcysteine conjugates of DBCP provides information on GSH mediated and cytochrome P 450 mediated bioactivation pathways in the expression of DBCP-induced toxicities. N-Acetylcysteine conjugates excreted in the urine of male Sprague-Dawley rats administered DBCP, C1D2-DBCP, C2D1-DBCP, C3D2-DBCP, or D5-DBCP (80 mg/kg) were purified by reverse-phase HPLC as their Me ester derivs. and characterized by fast atom bombardment tandem mass spectrometry. These metabolites were also converted to tert-butyldimethylsilyl ether derivs. and analyzed by gas chromatog.-mass spectrometry (GC-MS) to facilitate the identification of N-acetyl-S-(2,3-dihydroxypropyl)cysteine (I), an apparent regioisomer of I, 2-(S-(N-acetylcysteinyl))-1,3-propanediol (II), N-acetyl-S-(3-hydroxypropyl)cysteine (III), and N-acetyl-S-(3-chloro-2-hydroxypropyl)cysteine (IV). Metabolites I, II, and IV displayed quant. retention of deuterium, an observation consistent with the formation of episulfonium ion intermediate(s) in their biogenesis. Mercapturate III retained three atoms of deuterium from D5-DBCP, and two atoms of deuterium from the dideuterio analogs (C1D2-DBCP and C3D2-DBCP), thus invoking P 450 mediated formation of 2-bromoacrolein (2-BA) as an intermediate in the biogenesis of III. A mechanism is proposed in which conjugate addition of GSH to 2-BA, subsequent episulfonium ion formation, and addition of GSH afford 1,2-(diglutathion-S-yl)propanal. Glutathione mediated reduction is invoked to afford S-(3-hydroxypropyl)GSH which would be excreted in the urine as III. The quant. retention of deuterium from C1D2-DBCP or C3D2-DBCP was indicative of isotopically sensitive branching of P 450 metabolism at either C1 or C3 to afford 2-BA. C2D1 -DBCP showed a 30% retention of 1 deuterium atom in III; the loss of the deuterium is consistent with 2-BA formation, whereas the retention of one deuterium atom is indicative of the formation of metabolite III through GSH conjugation of either 2,3-dibromopropanal or 2-bromo-3-chloropropanal. These data indicate that III is a marker metabolite for the potent direct-acting mutagen, 2-BA, or its metabolic precursors 2,3-dibromopropanal or 2-bromo-3-chloropropanal. Therefore, evidence has been presented for bioactivation of DBCP by glutathione and cytochrome P 450 mediated mechanisms.
ST dibromochloropropane metab acetylcysteine conjugate cytochrome glutathione
IT Carcinogens
Mutagens
Urine
(acetylcysteine conjugates formation from dibromochloropropane in relation to cytochrome P 450 and glutathione)
IT 96-12-8, 1,2-Dibromo-3-chloropropane
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(acetylcysteine conjugates formation from dibromochloropropane in relation to cytochrome P 450 and glutathione)
IT 70-18-8, Glutathione, biological studies 9035-51-2, Cytochrome P450, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(acetylcysteine conjugates formation from dibromochloropropane in relation to cytochrome P 450 and glutathione)

IT 163086-04-2
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(acetylcysteine conjugates formation from dibromochloropropane in relation to cytochrome P 450 and glutathione)

IT 96-12-8DP, 1,2-Dibromo-3-chloropropane, metabolites **23127-40-4P**, N-Acetyl-S-(3-hydroxypropyl)cysteine 23255-33-6P, N-Acetyl-S-(2,3-dihydroxypropyl)cysteine 97729-49-2P
RL: MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(acetylcysteine conjugates formation from dibromochloropropane in relation to cytochrome P 450 and glutathione)

IT 75-56-9, Propylene oxide, reactions 106-89-8, Epichlorohydrin, reactions 556-52-5, Glycidol 616-91-1, N-Acetylcysteine 627-18-9
RL: RCT (Reactant)
(acetylcysteine conjugates synthesis)

IT 923-43-3P, N-Acetyl-S-(2-hydroxypropyl)cysteine
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L30 ANSWER 15 OF 38 CA COPYRIGHT 2002 ACS
AN 123:416 CA Full-text
TI Acrolein Mercapturates: Synthesis, Characterization, and Assessment of Their Role in the Bladder Toxicity of Cyclophosphamide
AU Ramu, Kumar; Fraiser, Lucy H.; Mamiya, Blain; Ahmed, Tamer; Kehrer, James P.
CS College of Pharmacy, University of Texas, Austin, TX, 78712-1074, USA
SO Chem. Res. Toxicol. (1995), 8(4), 515-24
CODEN: CRTOEC; ISSN: 0893-228X
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 34
AB Acrolein is the metabolite of cyclophosphamide (CP) believed to be involved in the bladder toxicity associated with this anticancer drug. The mechanism by which this extremely reactive intermediate is delivered to the bladder is not known. Glutathione (GSH) readily conjugates with acrolein, and the acrolein mercapturate S-(3-hydroxypropyl)-N- acetylcysteine (3-hydroxyPrMCA) has been found in the urine of animals and man given CP. The objectives of this study were to prepare and characterize synthetic stds. of the GSH acrolein adduct (3-oxopropyl)glutathione (3-oxoPrGSH), the acrolein mercapturates S-(3-oxopropyl)-N-acetylcysteine (3-oxoPrMCA) and 3-hydroxyPrMCA, and the S-oxidation product of 3-oxoPrMCA (3-oxoPrMCA S-oxide). In addition, the release of acrolein from, and the bladder toxicity of, these conjugates was determined 3-OxoPrGSH and 3-oxoPrMCA were prepared with a 99% yield by condensing acrolein with GSH and N-acetylcysteine, resp. 3-HydroxyPrMCA was prepared with a 63% yield by refluxing 3-chloropropanol and N-acetylcysteine in a basic medium. Oxidation of 3-oxoPrMCA with H2O2 was used to prepare 3-oxoPrMCA S-oxide. By decreasing the reaction time to 1 h, and adjusting the ratio of 3-oxoPrMCA to H2O2, the yield of 3-oxoPrMCA S-oxide was increased to 96%. The anhydrous aldehyde, 3-oxoPrMCA, afforded characteristic aldehydic proton resonances (1H NMR) in deuterated DMSO. New resonances were observed in deuterated water, indicating a 75% hydration of the aldehyde to the corresponding geminal diol. This phenomenon was enhanced with 3-oxoPrMCA S-oxide where .apprx.100% hydration of the aldehyde to the corresponding geminal diol was observed When incubated at 25° in 100 mM potassium phosphate buffer containing 1 M KCl, pH 8.0, 3-oxoPrMCA released .apprx.6% and 3-oxoPrMCA S-oxide released .apprx.16-18% of the theor. maximum yield of acrolein after 30 min, as indicated by an increase in absorbance at 210 nm and confirmed by trapping this aldehyde as a semicarbazone. There was less than a 2% yield of acrolein from 3-hydroxyPrMCA or 3-oxoPrGSH under similar conditions. At pH 7.4 the release of acrolein from 3-oxoPrMCA and 3-oxoPrMCA S-oxide was decreased by 50%. An assay where aldehydes are reacted with m-aminophenol in acid media produced fluorescence consistent with 72%, 46%, 23%, and 1% yields of acrolein from 3-oxoPrMCA S-oxide, 3-oxoPrMCA, 3-oxoPrGSH, and 3-hydroxyPrMCA, resp. These yields were unaffected by incubation in buffer for up to 2 h. Acrolein, 3-oxoPrMCA S-oxide, 3-oxoPrMCA and 3-oxoPrGSH, but not 3-hydroxyPrMCA, damaged the bladder dose-dependently when instilled intravesically in mice at concns. of 10-20 mM. Potency was acrolein > 3-oxoPrMCA S-oxide > 3-oxoPrMCA > 3-oxoPrGSH. These data support the possibility that a mercapturic acid may be involved in the bladder toxicity of CP.
ST acrolein mercapturate bladder toxicity cyclophosphamide
IT Bladder
(damage; synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)
IT Neoplasm inhibitors
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)
IT 107-02-8, Acrolein, biological studies

RL: ADV (Adverse effect, including toxicity); MFM (Metabolic formation); RCT (Reactant); BIOL (Biological study); FORM (Formation, nonpreparative)
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)

IT 140226-30-8P
RL: ADV (Adverse effect, including toxicity); MFM (Metabolic formation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)

IT **23127-40-4P** 124521-13-7P 140226-31-9P
RL: ADV (Adverse effect, including toxicity); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)

IT 50-18-0, Cyclophosphamide
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)

IT 616-91-1, N-Acetyl-L-cysteine 627-30-5, 3-Chloropropanol
RL: RCT (Reactant)
(synthesis, characterization, and assessment of the role of acrolein mercapturates in bladder toxicity of cyclophosphamide)

L30 ANSWER 16 OF 38 CA COPYRIGHT 2002 ACS
AN 122:230285 CA Full-text
TI Differential toxicities of cyclophosphamide and its glutathione metabolites to A549 cells
AU Perry, C. S.; Liu, X.; Lund, L. G.; Whitman, C. P.; Kehrer, J. P.
CS Coll. Pharm., Univ. Texas at Austin, Austin, TX, 78712-1074, USA
SO Toxicol. in Vitro (1995), 9(1), 21-6
CODEN: TIVIEQ; ISSN: 0887-2333
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Cyclophosphamide (CP), a widely used antineoplastic agent, is metabolized to species responsible for both the therapeutic and toxic effects of this drug. Acrolein is believed to be the primary toxic metabolite. This α,β-unsatd. aldehyde reacts rapidly with glutathione (GSH) and can then be further metabolized to mercapturic acid derivs. The toxicities of the acrolein-glutathione adduct 3-oxopropylglutathione (oxoPrGSH) and of the acrolein-mercapturic acid derivs. S-3-oxopropyl-N-acetylcysteine (oxoPrMCA) and S-3-hydroxypropyl-N- acetylcysteine (hydroxyPrMCA) have not been fully tested. OxoPrMCA, hydroxyPrMCA and oxoPrGSH were synthesized. The toxicities of these compds., along with those of CP and acrolein, were assessed by measuring their effects on the growth of human type II A549 lung carcinoma cells by using the alamarBlue assay. Each compound was incubated with A549 cells under serum-free conditions for 2 h, followed by an addnl. 94-h growth in the presence of fresh medium with serum. A 50% reduction in cell growth 72 h after treatment was produced by 83 μM oxoPrMCA or 4 μM acrolein. No significant toxicity was seen with hydroxyPrMCA (10 mM) or oxoPrGSH (5 mM). CP (5 mM) also had no effect on the growth of A549 cells under these conditions. This latter finding is consistent with previous evidence that CP requires metabolic activation to exert its toxicity. When present during the xenobiotic exposure, GSH (2 mM) almost completely protected against the growth inhibition caused by 1 mM oxoPrMCA or 10 μM acrolein. N-Acetylcysteine (1 mM) also prevented the toxicity caused by 1 mM oxoPrMCA and provided significant protection against the growth inhibition induced by 10 μM acrolein. These data support the concept that toxicity from oxoPrMCA may be due to the release of acrolein.
ST cyclophosphamide glutathione metabolite antitumor toxicity; acrolein cyclophosphamide metabolite antitumor toxicity
IT Neoplasm inhibitors
(glutathione metabolites of cyclophosphamide as)
IT 627-30-5, 3-Chloropropanol
RL: RCT (Reactant)
(reaction with N-acetylcysteine)
IT 50-18-0, Cyclophosphamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(toxicity of cyclophosphamide and its glutathione-derived metabolites)
IT 107-02-8, Acrolein, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); RCT (Reactant); BIOL (Biological study)
(toxicity of cyclophosphamide and its glutathione-derived metabolites)
IT **23127-40-4P** 124521-13-7P 140226-30-8P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(toxicity of cyclophosphamide and its glutathione-derived metabolites)
IT 70-18-8, Glutathione, biological studies
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);

BIOL (Biological study)
(toxicity of cyclophosphamide and its glutathione-derived metabolites)

IT 616-91-1, N-Acetylcysteine
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
BIOL (Biological study)
(toxicity of cyclophosphamide and its glutathione-derived metabolites
inhibition by)

L30 ANSWER 17 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 3
AN 118:162558 CA Full-text
TI Quantitative determination of N-acetyl-L-cysteine derivatives in human urine by tandem mass spectrometry
AU Stanek, W.; Krenmayr, P.; Schere, G.; Schmid, E. R.
CS Inst. Gen. Chem., Tech. Univ. Vienna, Vienna, A-1060, Austria
SO Biol. Mass Spectrom. (1993), 22(2), 133-42
CODEN: BIMSEH; ISSN: 1052-9306
DT Journal
LA English
CC 4-1 (Toxicology)
AB Collision-induced dissociation (CID) methods are described for the quantification of nanogram per mL (ppb) concns. of 2-acetamido-3-(3'-hydroxypropylthio)propanoic acid (I) and 2-acetamido-3-phenylthiopropanoic acid (II) in human urine exts. I and II are potential detoxification products of acrolein and benzene in conjugation with N-acetyl-L-cysteine derived from glutathione. The authors studied the potential of tandem mass spectrometry (MS/MS) under electron impact (EI) and chem. ionization (CI) conditions as a confirmatory screening technique for these compds. The main goals were high selectivity and low detection limits along with little or no sample clean-up. The effects of the mode of ionization and of collision conditions on the CID spectra were investigated. Direct insertion probe without any derivatization or short-column gas chromatog. separation techniques were used. Total instrument and data anal. time was about 15 min for direct insertion probe MS/MS and about 30 min for short-column GC/MS/MS. Detection limits are: direct insertion probe MS/MS (EI mode), 50 ppb (100 pg) for compound I; short-column GC/MS/MS (EI mode), 1.5 ppb (5 pg) for compound II; and short-column GC/MS/MS (CI mode), 0.6 ppb (2 pg) for the Me ester of compound II. Results are compared with non-mass spectrometric methods. The MS/MS methods were applied for the determination of I (EI mode) and II (CI mode) in urinary samples of a smoker and eight nonsmokers. After smoking, the urinary levels of I and II were elevated, whereas no increase was observed after exptl. passive smoking.
ST acetylcysteine deriv urine tandem mass spectrometry
IT Tobacco smoke and smoking
(acetylcysteine derivs. determination in human urine by tandem mass spectrometry in relation to)
IT Urine analysis
(for acetylcysteine derivs., in human, by tandem mass spectrometry)
IT 4775-80-8 **23127-40-4**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human urine by tandem mass spectrometry)

L30 ANSWER 18 OF 38 CA COPYRIGHT 2002 ACS
AN 118:191008 CA Full-text
TI New methods for computational ion structure evaluation by means of tandem mass spectrometry
AU Hayek, Erich W. H.; Stanek, Wolfgang; Krenmayr, Peter
CS Inst. Gen. Chem., Tech. Univ. Vienna, Vienna, A-1060, Austria
SO Rapid Commun. Mass Spectrom. (1993), 7(1), 99-105
CODEN: RCMSEF; ISSN: 0951-4198
DT Journal
LA English
CC 22-8 (Physical Organic Chemistry)
AB New methods are presented for the evaluation of ion structures and fragmentation pathways using tandem mass spectrometry (MS/MS) with low-energy collision-induced dissociation They incorporate a PC software package [named PDNL, written in Turbo-PASCAL 5.5 (Borland), running under DOS (Microsoft) with mouse control]. A database of almost 300 low-energy MS/MS spectra is available for library searches. It utilizes a new, intensity-based matching algorithm fitting the demand of MS/MS data. Computational methods have been developed for (i) the separation of the spectra of unresolved isobaric ions and evaluation of the ratio of the ion abundances, (ii) the evaluation of single-collision spectra using the multicollisional data map, and (iii) the elucidation of collision-induced dissociation fragmentation pathways. Principal component analyses of sets of at least 8 MS/MS spectra were used for a quick comparison of these spectra and for a summary of inter-ion relationships.
ST ion structure tandem mass spectrometry; computer evaluation ion structure tandem MS
IT Fragmentation reaction
(of ions in tandem mass spectrometry, computer application to)
IT Computer application
(to ion structure and fragmentation determination in tandem mass spectrometry)
IT Mass spectrometry
(tandem, ion structures and fragmentation paths in)
IT 616-91-1 4775-80-8 5572-21-4 15060-26-1 16637-59-5 19216-62-7 **23127-40-4** 51868-61-2 74514-75-3 130918-95-5
RL: PRP (Properties)
(tandem mass spectra of)

L30 ANSWER 19 OF 38 CA COPYRIGHT 2002 ACS
AN 117:27067 CA Full-text
TI Characterization of synthetic N-acetylcysteine conjugates by positive- and negative-ion californium-252Cf plasma desorption mass spectrometry
AU Pittenauer, Ernst; Pachinger, Anton; Allmaier, Guenter; Schmid, Erich R.
CS Inst. Anal. Chem., Univ. Vienna, Vienna, A-1090, Austria
SO Org. Mass Spectrom. (1991), 26(12), 1065-73
CODEN: ORMSBG; ISSN: 0030-493X
DT Journal
LA English
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 22
AB N-Acetylcysteine and nine N-acetylcysteine conjugates of synthetic origin were characterized by pos.- and neg.-ion plasma desorption mass spectrometry. For sample preparation, the electrospray technique and the nitrocellulose spin deposition technique were applied. The fragmentation of these compds., which are best seen as S-substituted desaminoglycylcysteine dipeptides, shows a similar behavior to that of linear peptides. In the pos.-ion mass spectra, intense protonated mol. ion peaks are observed In addition, several sequence-specific fragment ions (A+, B+, [Y + 2 H]+, Z+), immonium ions (I+) and a diagnostic fragment ion for mercapturic acids (RM+) are detected. The neg.-ion mass spectra exhibit deprotonated mol. ions and, in contrast, only one fragment ion corresponding to side-chain specific cleavage ([RXS]-) representing the xenobiotic moiety. In the case of a low alkali metal concentration on the target, cluster mol. ions of the [nM + H]+ or [nM - H]- ion type (n = 1-3) are observed The anal. of an equimolar mixture of eight N-acetylcysteine conjugates shows different quasimol. ion yields for the pos.- and neg.-ion spectra.
ST acetylcysteine conjugate mass spectra; neg ion mass spectra acetylcysteine
IT Mass spectra
(of acetylcysteine conjugates by)
IT Mass spectra
(neg.-ion, of acetylcysteine conjugates by plasma desorption)
IT 616-91-1, N-Acetylcysteine 4775-80-8 5572-21-4 15060-26-1 16637-59-5, N-Acetyl-S-methylcysteine 19216-62-7, N-Acetyl-S-butylcysteine **23127-40-4** 51868-61-2 74514-75-3 130918-95-5
RL: RCT (Reactant)
(pos.- and neg.-ion plasma desorption mass spectrometry of)

L30 ANSWER 20 OF 38 CA COPYRIGHT 2002 ACS
AN 115:176788 CA Full-text
TI Tandem mass spectrometric studies of mercapturic acid derivatives. Fragmentation, structure elucidation of fragment ions and development of an analytical method
AU Stanek, W.; Hayek, E. W. H.; Krenmayr, P.; Schmid, E. R.
CS Inst. Gen. Chem., Tech. Univ. Vienna, Vienna, A-1060, Austria
SO Fresenius. J. Anal. Chem. (1991), 340(4), 201-6
CODEN: FJACES; ISSN: 0937-0633
DT Journal
LA English
CC 4-1 (Toxicology)
AB The fragmentation of sixteen S-substituted N-acetyl(-1-)cysteine derivs. (mercapturic acids and Me esters) was studied under collision induced dissociation (CID) conditions recording series of product (daughter) ion spectra. After transfer of the data from the MS data system to an external PC, a PASCAL computer program called PDNL (Parent - Daughter - Neutral Loss) was used (a) to elucidate the structures of fragment ions by means of comparison with an MS/MS spectral library, (b) to construct an MS/MS data domain, (c) to eliminate consecutive decompns., (d) to evaluate the fragmentation pathways, and (e) to develop an MS/MS detector for mercapturic acids or their Me esters. In this way, common fragmentation reactions for mercapturic acids and their Me esters could be ascertained. Selected reaction monitoring using a direct insertion probe was used to determine the concentration of 3-hydroxypropylmercapturic acid in human urine. The limit of detection was 50 ppb (signal-to-noise ratio = 3:1) using 5 μL exts. from urine. This method was compared with a classical method for the quant. determination of another compound The relative standard deviation and the coefficient of variation are specified for the MS/MS method.
ST tandem mass spectrometry mercapturic acid deriv
IT Computer program
(for mercapturic acid derivs. determination)
IT Urine analysis
(for mercapturic acid derivs., in human)
IT Mass spectroscopy
(tandem, of mercapturic acid derivs.)
IT **23127-40-4**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human urine by tandem mass spectrometry)
IT 4775-80-8 5572-21-4 15060-26-1 16637-59-5 19216-62-7 51868-61-2 54322-43-9 60889-65-8 74514-75-3 77109-48-9 77549-18-9 89197-87-5 100496-03-5 102244-55-3 136590-37-9
RL: PRP (Properties)
(mass spectrometry of, tandem)

L30 ANSWER 21 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 4
AN 111:148250 CA Full-text
TI 3-Hydroxypropylmercapturic acid: a biologic marker of exposure to allylic and related compounds
AU Sanduja, Radhika; Ansari, G. A. S.; Boor, Paul J.
CS Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SO J. Appl. Toxicol. (1989), 9(4), 235-8
CODEN: JJATDK; ISSN: 0260-437X
DT Journal
LA English
CC 4-3 (Toxicology)
AB 3-Hydroxypropylmercapturic acid [3-OHPrMCA] was quant. measured by HPLC in the urine of rats given allylamine·HCl (5, 25, 50, 100, and 150 mg kg-1), acrolein (13 mg kg-1), allyl alc. (64 mg kg-1), allyl chloride (76 mg kg-1), allyl bromide (120 mg kg-1), allyl cyanide (115 mg), and cyclophosphamide (160 mg kg-1) by gavage in water. 3-OHPrMCA was measured by HPLC in 24-h urine collections; the lower detection limit was 1.25 μg or 5.6 nmol mL-1. Various doses of allylamine resulted in 3-OHPrMCA excretion at a fairly constant percentage of the dose, ca. 44-48% at 0-24 h and 3% at 24-48 h, indicating rapid metabolism through glutathione conjugation in the first 24 h. Similarly, 3-OHPrMCA was recovered in the urine of rats given acrolein (78.5%), allyl alc. (28.3%), allyl chloride (21.5%), allyl bromide (3.0%), allyl cyanide (3.7%), and cyclophosphamide (2.6%). These data indicate that 3-OHPrMCA can be used as a marker of exposure to allylic and other compds. that lead to the metabolic formation of acrolein.
ST hydroxypropylmercapturate urine allylic compd
IT Urine
(hydroxypropylmercapturic acid of, as allylic compound metabolite)
IT Allylic compounds
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, urinary hydroxypropylmercapturic acid as marker for)
IT 50-18-0, Cyclophosphamide 106-95-6, Allylbromide, biological studies 107-02-8, Acrolein, biological studies 107-05-1, Allylchloride 107-11-9, Allylamine 107-18-6, Allylalcohol, biological studies 109-75-1, Allylcyanide
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, urinary hydroxypropylmercapturic acid as marker for)
IT **23127-40-4**
RL: BIOL (Biological study)
(of urine, as allylic compound metabolite)

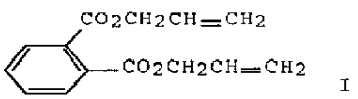
L30 ANSWER 22 OF 38 CA COPYRIGHT 2002 ACS
AN 110:19508 CA Full-text
TI Disposition of inhaled 1-chloro-2-propanol in F344/N rats
AU Bond, James A.; Birnbaum, Linda S.; Dahl, Alan R.; Medinsky, Michele A.; Sabourin, Patrick J.; Henderson, Rogene F.
CS Inhalation Toxicol. Res. Inst., Lovelace Biomed. Environ. Res. Inst., Albuquerque, NM, 87185, USA
SO Toxicol. Appl. Pharmacol. (1988), 95(3), 444-55
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
CC 4-3 (Toxicology)
AB The objective of these studies was to determine whether changes in the inhaled exposure concentration would affect the disposition of 1-chloro-2-propanol (1-CP) in rats. In addition, expts. were conducted to identify the carbon atom of 1-CP that is metabolized to CO2. Rats were exposed nose-only to [14C]1-CP for 6 h to 8.3 ppm (26.1 μg/L air) or 77 ppm (145 mg/L air). There were two major routes of elimination of 14C, urinary and exhalation of CO2, which together accounted for .apprx.80% of the total 14C in excreta and carcass. Half-times for elimination of 14C in urine and as 14CO2 were between 3 and 7 h with no effect of exposure concentration on the elimination half-times for either route. After the end of exposure, kidneys, livers, trachea, and nasal turbinates contained high concns. of [14C]1-CpP equivalent at both exposure concns. (30-50 nmol 14C/g tissue for the 8 ppm exposure level and 200-350 nmol 14C/g tissue for the 80 ppm exposure level). Elimination of 14C from tissues biphasic with about 50% of the material in a tissue being rapidly eliminated with a half-time of 1 to 3 h and the remaining material slowly eliminated with a half-time of 40 to 80 h. There was no effect of exposure concentration on elimination half-times in tissues. Major metabolites detected in urine and tissues (liver, kidney, and lung) were N-acetyl-S-(hydroxypropyl)cysteine and(or)S-(2- hydroxypropyl)-cysteine. Little unmetabolized 1-CP (<1%) was detected in tissues or urine. A metabolic scheme is proposed in which the major pathway for metabolism of 1-CP is to CO2 (which is exhaled) and to cysteine conjugates and mercapturic acids that are excreted in the urine. Both carbon-2 and carbon-3 are metabolized in part to CO2.
ST chloropropanol metab
IT Air, respiratory
Bile
Blood
Feces
Urine
(chloropropanol in, metabolism in relation to)
IT Kidney, metabolism
Liver, metabolism
Lung, metabolism
Organ
Spleen, metabolism
Trachea (anatomical)
(chloropropanol metabolism by)
IT Bone, metabolism
(turbinate, chloropropanol metabolism by)
IT 78-95-5, Chloroacetone 6367-97-1 **23127-40-4**
RL: BIOL (Biological study)
(chloropropanol metabolite, of body fluid and organ)
IT 127-00-4, 1-Chloro-2-propanol
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, after inhalation)

L30 ANSWER 23 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1988:506230 BIOSIS Full-text
DN BA86:126914
TI HEPATOTOXICITY OF CYCLOPHOSPHAMIDE IN MAN PHARMACOKINETIC ANALYSIS.
AU HONJO I; SUOU T; HIRAYAMA C
CS SECOND DEP. INTERN. MED., TOTTORI UNIV. SCH. MED., YONAGO 683, JAPAN.
SO RES COMMUN CHEM PATHOL PHARMACOL, (1988) 61 (2), 149-166.
CODEN: RCOCB8. ISSN: 0034-5164.
FS BA; OLD
LA English
AB Of 44 patients with neoplasia treated with cyclophosphamide (CPA), 19 (43%) had a transient elevation of serum levels of aminotransferases. In these patients, regardless of the combination chemotherapy regimen given, the incidence of liver dysfunction was 33%, when the total CPA dose was less than 400 mg/m2 (Group A) and 73% with higher doses (Group B). Prior to the initiation of CPA treatment, pharmacokinetics of CPA were investigated in 15 patients. Plasma AUCs of CPA and phosphoramide mustard (PM) in 8 patients in Group B were higher than those in 7 Group A patients. In contrast, urinary excretion of 3-hydroxypropylmercapturic acid (3-HPMCA) was lower in Group B than in Group A. The ratio of urinary 3-HPMCA to plasma AUC of PM was significantly lower in Group B than in Group A ($p < 0.05$). These results indicate that CPA-induced liver injury is mainly dose-dependent and presumably results from impaired metabolism of CPA, and especially of its metabolite, acrolein.
CC Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Metabolism - General Metabolism; Metabolic Pathways *13002
Metabolism - Metabolic Disorders *13020
Digestive System - Pathology *14006
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology *22005
Toxicology - Pharmacological Toxicology *22504
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Hominidae 86215
IT Miscellaneous Descriptors
ANTINEOPLASTIC AGENT NEOPLASIA AMINOTRANSFERASE LIVER DYSFUNCTION 3 HYDROXYPROPYLMERCAPTURIC ACID ACROLEIN METABOLIC DYSFUNCTION METABOLITE DOSE DEPENDENCE
RN 50-18-0 (CYCLOPHOSPHAMIDE)
107-02-8 (ACROLEIN)
9031-66-7 (AMINOTRANSFERASE)
23127-40-4 (3 HYDROXYPROPYLMERCAPTURIC ACID)

L30 ANSWER 24 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 5
AN 108:70296 CA Full-text
TI In vivo metabolism of the cardiovascular toxin, allylamine
AU Boor, Paul J.; Sanduja, Radhika; Nelson, Thomas J.; Ansari, G. A. S.
CS Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SO Biochem. Pharmacol. (1987), 36(24), 4347-53
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
CC 4-3 (Toxicology)
AB 3-Hydroxypropylmercapturic acid was isolated and identified as the sole urinary metabolite of allylamine metabolism in vivo. Parallel expts. showed GSH depletion in several organs (most marked in aorta, blood, and lung), which is consistent with GSH conjugation of the proposed acrolein intermediate. Apparently allylamine was metabolized in vivo to a highly reactive aldehyde which was converted to a mercapturic acid through a GSH conjugation pathway.
ST allylamine metab GSH
IT Blood
Brain, composition
Heart, composition
Kidney, composition
Organ
(glutathione of, allylamine metabolism effect on)
IT Urine
(hydroxypropylmercapturic acid of, allylamine metabolism in relation to)
IT Artery, composition
(aorta, glutathione of, allylamine metabolism effect on)
IT 107-02-8, Acrolein, biological studies
RL: BIOL (Biological study)
(as allylamine metabolite, glutathione depletion in relation to)
IT 70-18-8, Glutathione, biological studies
RL: BIOL (Biological study)
(depletion of, of organs, allylamine metabolism induction of)
IT 107-11-9, Allylamine
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, hydroxypropylmercapturic acid formation by, glutathione depletion in relation to)
IT **23127-40-4**, 3-Hydroxypropylmercapturic acid
RL: BIOL (Biological study)
(of urine, as allylamine metabolite)
IT 13189-98-5P, S-(3-Hydroxypropyl)-L-cysteine **23127-40-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L30 ANSWER 25 OF 38 CA COPYRIGHT 2002 ACS
AN 104:103750 CA Full-text
TI Identification and quantitative determination of four different mercapturic acids formed from 1,3-dibromopropane and its 1,1,3,3-tetradeutero analog by the rat
AU Onkenhout, W.; Van Bergen, E. J. C.; Van der Wart, J. H. F.; Vos, G. P.; Buijs, W.; Vermuelen, N. P. E.
CS Dep. Pharm. Anal., State Univ. Leiden, Leiden, 2300, Neth.
SO Xenobiotica (1986), 16(1), 21-33
CODEN: XENOBH; ISSN: 0049-8254
DT Journal
LA English
CC 4-3 (Toxicology)
AB 1,3-Dibromopropane (I) [109-64-8] was administered i.p. in doses ranging from 5.6 mg to 54 mg to male rats. Total amts. of mercapturic acids excreted in the urine varied considerably among different rats. In contrast to previous investigation that indicated N-acetyl-S-3- hydroxypropyl(l-)cysteine [**23127-40-4**] as a major metabolite in the rat (Jones, A. R., Wells, G., 1981), this metabolite was excreted only in trace amts. (0.2% dose of 54 mg of I) in 28 h urine. Instead N-acetyl-S-3-bromopropyl-(L)-cysteine (II) [78093-70-6] and surprisingly N-acetyl-S-3-chloropropyl-(L)-cysteine (III) [100496-00-2] were identified as the major metabolites. Recovery of II added to normal rat urine, kept for 24 h at room temperature, led to III as the major decomposition product. Apparently, II was converted to III in urine. The retention of 4 2H atoms in III after dosing with 1,1,3,3-tetradeutero-1,3- dibromopropane [64528-94-5] is in accordance with the mechanism that II is transformed into III via an episulfonium ion. The excretion of another metabolite N-acetyl-S-2-carboxyethyl-(L)-cysteine [51868-61-2] was delayed.
ST bromopropane metab mercapturate urine
IT Urine
(mercapturic acid metabolites of, dibromopropane metabolism in relation to)
IT 64528-94-5
RL: BIOL (Biological study)
(mercapturic acid metabolites of urine response to, dibromopropane metabolism in relation to)
IT 109-64-8
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, mercapturates identification in urine response to)
IT **23127-40-4** 51868-61-2 78093-70-6 100496-00-2
RL: BIOL (Biological study)
(of urine, dibromopropane metabolism in relation to)
IT 85680-04-2P 100496-01-3P 100496-02-4P 100496-03-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, dibromopropane metabolites identification in urine in relation to)
IT 616-91-1
RL: RCT (Reactant)
(reaction of, mercapturic acid derivs. preparation in relation to)
IT 79-10-7, reactions 109-64-8 627-30-5 6940-76-7
RL: RCT (Reactant)
(reaction of, with acetylcysteine)
IT 18358-13-9, reactions
RL: RCT (Reactant)
(reaction of, with acetylcysteine Me ester)

L30 ANSWER 26 OF 38 CA COPYRIGHT 2002 ACS
AN 106:14316 CA Full-text
TI Examination of the differential hepatotoxicity of diallyl phthalate in rats and mice
AU Eigenberg, David A.; Carter, Dean E.; Schram, Karl H.; Sipes, I. Glenn
CS Coll. Pharm., Univ. Arizona, Tucson, AZ, 85721, USA
SO Toxicol. Appl. Pharmacol. (1986), 86(1), 12-21
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
CC 4-3 (Toxicology)
GI



I

AB Higher hepatotoxicity of diallyl phthalate (DAP)(I) [131-17-9] to rats than mice was confirmed and the same species difference in the toxicity for allyl alc. (AA) [107-18-6] was demonstrated. The toxicity of DAP probably results from AA cleaved from DAP. To determine if the species difference in susceptibility to hepatotoxicity resulted from differences in the disposition and metabolism of DAP, Fischer-344 rats and B6C3F1 mice were orally given [14C]DAP, 1, 10, or 100 mg/kg or 10 mg/kg i.v., and placed in metabolism cages for 24 h. In rats, 25-30% of the DAP was excreted as CO2, and 50-70% appeared in the urine within 24 h. In mice, 6-12% of the DAP was excreted as CO2, and 80-90% was excreted in the urine within 24 h. Monoallyl phthalate (MAP) [3882-14-2], allyl alc., 3-hydroxypropylmercapturic acid (HPMA) [**23127-40-4**], and an unidentified polar metabolite (PM) were found in the urine of rats and mice dosed with DAP. The PM was present in the urine of rats dosed with DAP or AA, indicating that the compound is a metabolite of AA. There was no difference between the species in the quantity of AA excreted, but mice excreted more MAP (39 vs. 33%), HPMA (28 vs. 17%), and PM (20 vs. 8%) than rats. Because DAP is metabolized to AA, a potent periportal hepatotoxicant, and because the mouse produced more HPMA than rats, the differential hepatotoxicity of DAP may be related to the extent of glutathione [70-18-8] conjugation with allyl alc. or acrolein (the active metabolite of AA).
ST allyl phthalate hepatotoxicity species; allyl alc phthalate hepatotoxicity species
IT Liver, toxic chemical and physical damage
(allyl alc. and diallyl phthalate toxicity to, species differences in relation to)
IT Brain, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Muscle, metabolism
Organ
Skin, metabolism
Testis, metabolism
(diallyl phthalate metabolism by)
IT Urine
(diallyl phthalate metabolites of, species difference in relation to)
IT Blood

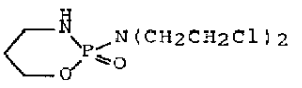
(diallyl phthalate of)
IT Intestine, metabolism
(small, diallyl phthalate metabolism by)
IT 70-18-8, Glutathione, biological studies
RL: PRP (Properties)
(conjugation of, with allyl alc., diallyl phthalate hepatotoxicity species difference in relation to)
IT 124-38-9, biological studies
RL: BIOL (Biological study)
(diallyl phthalate metabolite, hepatotoxicity and species difference in relation to)
IT 107-18-6, Allyl alcohol, biological studies 3882-14-2, Monoallyl phthalate **23127-40-4**, 3-Hydroxypropylmercapturic acid
RL: BIOL (Biological study)
(diallyl phthalate metabolite, hepatotoxicity in species difference in relation to)
IT 131-17-9D, Diallyl phthalate, metabolites
RL: BIOL (Biological study)
(hepatotoxicity and species difference in relation to)
IT 9000-86-6
RL: BIOL (Biological study)
(of serum, allyl alc. and diallyl phthalate effect on)
IT 131-17-9, Diallyl phthalate
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to liver, species difference in relation to)

L30 ANSWER 27 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 6
AN 96:156811 CA Full-text
TI The metabolism of 1,3-dibromopropane by the rat
AU Jones, A. R.; Wells, G.
CS Dep. Biochem., Univ. Sydney, Sydney, 2006, Australia
SO Xenobiotica (1981), 11(8), 541-6
CODEN: XENOBH; ISSN: 0049-8254
DT Journal
LA English
CC 4-3 (Toxicology)
AB Studies of the metabolism of 1,3-dibromopropane (I)) [109-64-8] in the rat enabled identification of 2 conjugated metabolites in urine as S-(3-hydroxypropyl)cysteine [13189-98-5] and N-acetyl-S-(3- hydroxypropyl)cysteine **[23127-40-4]**. An oxidation product, β-bromolactic acid [32777-03-0] was isolated as a urinary metabolite. I was not excreted unchanged in expired air or in the urine. Approx. 15% of the dose (100 mg/kg) was excreted as metabolic products over 50 h and 3.5% as CO2 within 6 h indicating that oxidation is the main route of detoxication.
ST dibromopropane metab
IT 13189-98-5 **23127-40-4** 32777-03-0
RL: BIOL (Biological study)
(as dibromopropane metabolite)
IT 109-64-8
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of)

L30 ANSWER 28 OF 38 MEDLINE
AN 81128454 MEDLINE Full-text
DN 81128454 PubMed ID: 7467399
TI 1,2-Dichloropropane: metabolism and fate in the rat.
AU Jones A R; Gibson J
SO XENOBIOTICA, (1980 Nov) 10 (11) 835-46.
Journal code: 1306665. ISSN: 0049-8254.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198104
ED Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810424
AB 1. The metabolism of 1,2-dichloropropane in the rat has been investigated. The major urinary metabolite has been isolated and identified as N-acetyl-S-(2-hydroxypropyl)cysteine. Two minor metabolites of 1,2-dichloropropane have been identified as beta-chlorolactate and N-acetyl-S-(2,3-dihydroxypropyl)cysteine. 2. The fate of 1-chloro-2-hydroxypropane, a proposed intermediate metabolite of 1,2-dichloropropane, has been investigated. Apart from its known urinary metabolite, N-acetyl-S-(2-hydroxypropyl)cysteine, two oxidative metabolites were detected. These were identified as beta- chlorolactaldehyde and beta-chlorolactate. 3. A pathway is proposed for the metabolism and fate of 1,2-dichloropropane in the rat. This accounts for previous observations made for the fate of radioactivity from administration of 1,2-dichloro[1-14C]propane. 4. The microbial and mammalian metabolism of several halogen-containing foreign compounds is discussed.
CT Check Tags: Animal; Male
Acetylcysteine: AA, analogs & derivatives
Acetylcysteine: UR, urine
Chlorohydrins: UR, urine
Hydrocarbons, Chlorinated: UR, urine
*Liver: ME, metabolism
Metabolic Detoxication, Drug
Models, Chemical
*Propane: AA, analogs & derivatives
Propane: UR, urine
Rats
Sulfhydryl Compounds: ME, metabolism
RN 127-00-4 (1-chloro-2-propanol); **23127-40-4 (S-(3-hydroxypropyl)cysteine N-acetate)**; 616-91-1 (Acetylcysteine); 74-98-6 (Propane); 78-87-5 (propylene dichloride)
CN 0 (Chlorohydrins); 0 (Hydrocarbons, Chlorinated); 0 (Sulfhydryl Compounds)

L30 ANSWER 29 OF 38 CA COPYRIGHT 2002 ACS
AN 92:175112 CA Full-text
TI The oxidative metabolism of 1-bromopropane in the rat
AU Jones, A. R.; Walsh, D. A.
CS Dep. Biochem., Univ. Sydney, Sydney, 2006, Australia
SO Xenobiotica (1979), 9(12), 763-72
CODEN: XENOBH; ISSN: 0049-8254
DT Journal
LA English
CC 3-5 (Biochemical Interactions)
AB Rats metabolized 1-bromopropane [106-94-5] to N-acetyl-S-propylcysteine [14402-54-1], N-acetyl-S-propylcysteine S-oxide [1424-26-6], N-acetyl-S-(2-hydroxypropyl)cysteine [923-43-3], 3-bromopropionic acid [590-92-1], N-acetyl-S-(3-hydroxypropyl)cysteine (I) [**23127-40-4**], and N-acetyl-S-(2-carboxyethyl)cysteine (II) [51868-61-2]. They also metabolized 3-bromopropanol [627-18-9] and 3-chloropropanol [627-30-5] to I and II and to the corresponding 2-carboxyethyl halides. Studies with 1-bromopropane and the 3-halopropanols in vitro indicated that oxidation of C3 and C2 of 1-bromopropane occurred before conjugation of the alkyl group with glutathione.
ST bromopropane metab; propane bromo metab
IT 590-92-1 923-43-3 1424-26-6 14402-54-1 **23127-40-4**
51868-61-2
RL: PRP (Properties)
(as bromopropane metabolite)
IT 627-18-9 627-30-5
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of)
IT 106-94-5
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, to mercapturic acids)

L30 ANSWER 30 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 7
AN 92:190981 CA Full-text
TI The biosynthesis of 3-hydroxypropylmercapturic acid from cyclophosphamide
AU Giles, P. M.
CS Dep. Biochem., St. Thomas's Hosp. Med. Sch., London, Engl.
SO Xenobiotica (1979), 9(12), 745-62
CODEN: XENOBH; ISSN: 0049-8254
DT Journal
LA English
CC 1-2 (Pharmacodynamics)
GI



II

AB 3-Hydroxypropylmercapturic acid (I) [**23127-40-4**] was identified in the urine of rats dosed with cyclophosphamide (II) [50-18-0] (100-200 mg/kg, i.p., s.c., or by gavage), isophosphamide [3778-73-2] (200 mg/kg, i.p.), or trilophosphamide [22089-22-1] (150 mg/kg, i.p.), and was isolated as its dicyclohexylammonium salt from rats dosed with II. Rats excreted in their urine 55.5% of the 14C of an i.p. dose (200 mg/kg) of II-4-14C during the first 24 h after administration, and a further 6.6% during the next 24 h. Of the total radioactivity excreted during the first 24 h, unchanged II represented ≤19.3%, 41.6% was due to the major metabolite, carboxyphosphamide [22788-18-7], and I represented 11.9%. The 14C label in I was located in the S-substituent. I was the only S-containing metabolite of II found in the blood and liver of rats, but 14C-labeled I and S-(3-hydroxypropyl)-L-cysteine (III) [13189-98-5] were tentatively identified in the bile of rats dosed with 120 mg II-14C/kg, i.p. I and III were formed in the liver of rats dosed with allyl alc. [107-18-6]. Acrolein [107-02-8] underwent a complex reaction with GSH [70-18-8] in vitro, the major product of which was S-(3-hydroxypropyl)glutathione [73605-93-3]. The latter and III were both metabolized by the rat to I and 2 minor metabolites. I was converted by the rat to 2-carboxyethylmercapturic acid [51868-61-2] and one other metabolite; neither of these metabolites was found in the urine of rats dosed with II. A possible path for I formation from II is discussed.
ST cyclophosphamide metab hydroxypropylmercapturate
IT Liver, metabolism
(cyclophosphamide metabolism by, to hydroxypropylmercapturic acid)
IT 13189-98-5 22788-18-7 **23127-40-4**
RL: BIOL (Biological study)
(as cyclophosphamide metabolite)
IT 51868-61-2
RL: BIOL (Biological study)
(as hydroxypropylmercapturic acid metabolite)
IT 73605-93-3
RL: FORM (Formation, nonpreparative)
(formation of, from acrolein reaction with glutathione, cyclophosphamide metabolism in relation to)
IT 107-18-6, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, by liver)
IT 50-18-0 3778-73-2 22089-22-1

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, to hydroxypropylmercapturic acid)

IT 70-18-8, biological studies
RL: RCT (Reactant)
(reaction of, with acrolein, cyclophosphamide metabolism in relation to)

IT 107-02-8, biological studies
RL: RCT (Reactant)
(reaction of, with glutathione, cyclophosphamide metabolism in relation to)

L30 ANSWER 31 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1980:47818 BIOSIS Full-text
DN BR18:47818
TI CYCLO PHOSPHAMIDE INDUCED CYSTITIS ITS CAUSE AND POSSIBLE CLINICAL SIGNIFICANCE.
AU COX P J; ABEL G
CS DEP. BIOCHEM. PHARMACOL., CHESTER BEATTY RES. INST., LONDON SW3, ENGL., UK.
SO 20TH ANNUAL MEETING OF THE BRITISH ASSOCIATION FOR CANCER RESEARCH, GLASGOW, SCOTLAND, MAR. 28-30, 1979. BR J CANCER. (1979) 40 (2), 311. CODEN: BJCAAI. ISSN: 0007-0920.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease 12508
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Other Body Fluids 15010
Urinary System and External Secretions - Pathology *15506
Pharmacology - Urinary System *22032
Toxicology - Pharmacological Toxicology *22504
Toxicology - Antidotes and Preventative Toxicology *22505
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Chemotherapy - General; Methods; Metabolism *38502
Pest Control, General; Pesticides; Herbicides 54600
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT RAT N ACETYL-L CYSTEINE IFOSFAMIDE PHOSPHORAMIDE MUSTARD NORNITROGEN MUSTARD 5 5 DI METHYL CYCLO PHOSPHAMIDE DI ETHYLAMINE DI ETHYL CYCLO PHOSPHAMIDE ACROLEIN 3 HYDROXYPROPYL MERCAPTURIC-ACID EDEMA HEMORRHAGE
RN 50-18-0 (CYCLO PHOSPHAMIDE)
107-02-8 (ACROLEIN)
109-89-7 (DI ETHYLAMINE)
334-22-5 (NORNITROGEN MUSTARD)
616-91-1 (N ACETYL-L CYSTEINE)
3778-73-2 (IFOSFAMIDE)
10159-53-2 (PHOSPHORAMIDE MUSTARD)
22089-27-6 (5 5 DI METHYL CYCLO PHOSPHAMIDE)
23127-40-4 (3 HYDROXYPROPYL MERCAPTURIC-ACID)

L30 ANSWER 32 OF 38 CA COPYRIGHT 2002 ACS DUPLICATE 8
AN 86:37554 CA Full-text
TI Studies on the in vivo formation of acrolein. 3-Hydroxypropylmercapturic acid as an index of cyclophosphamide (NSC-26271) activation
AU Alarcon, R. A.
CS Dep. Biol. Chem., Harvard Med. Sch., Boston, Mass., USA
SO Cancer Treat. Rep. (1976), 60(4), 327-35
CODEN: CTRRDO
DT Journal
LA English
CC 1-5 (Pharmacodynamics)
AB 3-Hydroxypropylmercapturic acid (MCA) was determined in the urine of rats given cyclophosphamide (I), related antineoplastic agents, allyl alc., or acrolein. Male rats injected with I (50 mg/kg) excreted 16.7 μmols of MCA/kg in their 24 h urine. Equivalent isophosphamide, triphosphamide, ASTA-5607, ASTA-5122, and cytoxyl alc. produced 9.0, 16.1, 4.1, and 0.4 μmols MCA/kg, resp. After administration of allyl alc. and acrolein, 26.3 and 19.7 μmols MCA/kg were obtained. MCA values were directly proportional to the drug doses given. Since acrolein and phosphorodiamidic acid mustard are the toxic decomposition products of aldophosphamide, and acrolein conjugation with glutathione appears to be the first step for MCA formation, values for MCA would reflect active I levels. The in vitro interaction of acrolein with glutathione, other sulfhydryl compds., and a few amino acids at concns. of 0.15 μmols./ml was also studied. The faster interactions observed were with the sulfhydryl compds.; a 50% decrease of acrolein absorption was observed in interactions with glutathione and cysteine (at pH 7.4 and 23°) in 111 and 30 sec, resp. Incubation of these acrolein-adducts at 37° and 100° generated acrolein with maximum recovery yield of 83% at 100°. Five patients given 1 g of I (i.v.) excreted 6.4-50.0 μmols MCA in their urine in 6 h.
ST hydroxypropylmercapturic acid cyclophosphamide activation; acrolein cyclophosphamide activation
IT 59866-10-3 59866-11-4 59866-12-5
RL: BIOL (Biological study)
(acrolein formation from, hydroxypropylmercapturic acid formation in relation to)
IT 13189-98-5
RL: FORM (Formation, nonpreparative)
(formation of, from acrolein-cysteine adduct)
IT 50-18-0 107-02-8, biological studies 107-18-6, biological studies 3778-73-2 14504-75-7 22089-22-1 37752-36-6 37753-10-9
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, hydroxypropylmercapturic acid formation in)
IT **23127-40-4**
RL: BIOL (Biological study)
(of urine, cyclophosphamide and related antineoplastic agents metabolism in relation to)
IT 70-18-8, reactions 616-91-1
RL: RCT (Reactant)
(reaction of, with acrolein, hydroxypropylmercapturic acid formation in relation to)
IT 56-40-6, reactions 56-45-1, reactions 63-68-3, reactions 74-79-3, reactions
RL: RCT (Reactant)
(with acrolein)
IT 52-90-4, reactions
RL: RCT (Reactant)
(with acrolein, hydroxypropylmercapturic acid formation in relation to)

L30 ANSWER 33 OF 38 CA COPYRIGHT 2002 ACS
AN 82:10986 CA Full-text
TI Acrolein as a possible metabolite of cyclophosphamide in man
AU Kaye, Clive M.; Young, Leslie
CS Dep. Biochem., St. Thomas's Hosp. Med. Sch., London, Engl.
SO Biochem. Soc. Trans. (1974), 2(2), 308-10
CODEN: BCSTB5
DT Journal
LA English
CC 1-2 (Pharmacodynamics)
GI For diagram(s), see printed CA Issue.
AB 3-(Hydroxypropyl)mercapturic acid (I) [**23127-40-4**] was detected in the urine of human patients and rats receiving cyclophosphamide (II) [50-18-0] (2-3 x 50 mg/day, orally and 20 mg, s.c. resp.). Since administration of acrolein [107-02-8] to rats gave (I) in the urine, acrolein may be metabolite of I in man.
ST acrolein cyclophosphamide metab
IT 107-02-8, biological studies **23127-40-4**
RL: BIOL (Biological study)
(as cyclophosphamide metabolite)
IT 50-18-0
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, acrolein formation in)

L30 ANSWER 34 OF 38 CA COPYRIGHT 2002 ACS
AN 80:78787 CA Full-text
TI Biosynthesis of mercapturic acids from allyl alcohol, allyl esters, and acrolein
AU Kaye, Clive M.
CS Dep. Biochem., St. Thomas's Hosp. Med. Sch., London, Engl.
SO Biochem. J. (1973), 134(4), 1093-101
CODEN: BIJOAK
DT Journal
LA English
CC 3-5 (Biochemical Interactions)
AB Mercapturic acids were detected in the urine of rats following the administration of various allyl esters, indicating that the animals were capable of such in vivo synthesis. Allyl alcohol [107-18-6], acrolein [107-02-8], and S-(3-hydroxypropyl)-L-cysteine [13189-98-5] were also converted to mercapturic acids. Allyl esters could be metabolized by acyl-oxygen fission or alkyl-oxygen fission to yield 3- hydroxypropylmercapturic acid [**23127-40-4**] or allylmercapturic acid [23127-41-5], resp. The latter occurred only when the ester was formed from a strong acid with a pka value of less than about 2.
ST mercapturic acid allyl ester
IT Bile
Urine
(mercapturic acids of, as allyl ester metabolites)
IT **23127-40-4**
RL: FORM (Formation, nonpreparative)
(formation of, from allyl ester)
IT 131-17-9 583-04-0 591-87-7 1623-19-4 2408-20-0 6289-31-2 19037-59-3 23127-41-5 31001-65-7
RL: FORM (Formation, nonpreparative)
(formation of, from allyl esters)
IT 16770-74-4
RL: PRP (Properties)
(mercapturic acid formation from)
IT 107-02-8, biological studies 107-18-6, biological studies
RL: BIOL (Biological study)
(mercapturic acids formation from)
IT 1838-59-1
RL: PRP (Properties)
(mercapturic acids formation from)
IT 13189-98-5P
RL: PREP (Preparation)
(preparation of)

L30 ANSWER 35 OF 38 CA COPYRIGHT 2002 ACS
AN 77:122712 CA Full-text
TI Metabolic formation of mercapturic acids from allyl halides
AU Kaye, C. M.; Clapp, J. J.; Young, L.
CS Dep. Biochem., St. Thomas's Hosp. Med. Sch., London, Engl.
SO Xenobiotica (1972), 2(2), 129-39
CODEN: XENOBH
DT Journal
LA English
CC 4-3 (Toxicology)
Section cross-reference(s): 3
AB Allylmercapturic acid [23127-41-5] was isolated from the urine of rats dosed with allyl chloride [107-05-1], and S-allyl-L-cysteine [21593-77-1] was a metabolite of allyl bromide [106-95-6], allyl iodide [556-56-9], and S-allylglutathione [23127-42-6]. The sulfoxide of allylmercapturic acid was detected in the urine of all animals which excreted allylmercapturic acid. 3-Hydroxypropylmercapturic acid [**23127-40-4**] was identified by gas-liquid chromatog. as a metabolite of allyl chloride and probably of the bromide and iodide. S-allylglutathione and S-allyl-L-cysteine were detected in the bile of rats dosed with allyl chloride. The mechanism of the biosynthesis of mercapturic acids from allyl halides was discussed.
ST allyl halide metab allylmercapturate; mercapturate allyl halide metab
IT Bile
Urine
(allyl halide metabolites of)
IT 23127-41-5
RL: FORM (Formation, nonpreparative)
(formation of, as allyl chloride metabolite)
IT **23127-40-4** 38131-20-3
RL: FORM (Formation, nonpreparative)
(formation of, as allyl halide metabolite)
IT 21593-77-1
RL: FORM (Formation, nonpreparative)
(formation of, as allylglutathione and allyl halide metabolite)
IT 106-95-6 107-05-1 556-56-9 23127-42-6
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of)
IT 13189-98-5P 14369-42-7P 38130-85-7P 38130-86-8P 38130-87-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L30 ANSWER 36 OF 38 CA COPYRIGHT 2002 ACS
AN 77:110005 CA Full-text
TI Synthesis of mercapturic acids from allyl compounds in the rat
AU Kaye, C. M.; Young, L.
CS Dep. Biochem., St. Thomas's Hosp., Med. Sch., London, Engl.
SO Biochem. J. (1972), 127(5), 87P
CODEN: BIJOAK
DT Journal
LA English
CC 3-5 (Biochemical Interactions)
AB Mercapturic acids were detected in the urine of rats dosed with allyl compds. Allyl formate [1838-59-1] and allyl propionate [2408-20-0] gave S-(3-hydroxypropyl)mercapturic acid (I) [**23127-40-4**] in 6.8 and 9.1% yield resp. Diallyl phthalate [131-17-9], allyl nitrite [31001-65-7], allylamine [107-11-9], allyl cyanide [109-75-1] gave I but allyl nitrate [16770-74-4] gave 2.6% I and 5.9% S-allylmercapturic acid [23127-41-5]. Administration of acrolein (II) [107-02-8] led to 10.5% I in the urine, suggesting II as an intermediate in the metabolic conversion of allyl alc. into a mercapturic acid.
ST mercapturate allyl compd metab; acrolein allyl alc mercapturate
IT **23127-40-4** 23127-41-5
RL: FORM (Formation, nonpreparative)
(formation of, from allyl compound metabolism)
IT 107-02-8, biological studies 107-11-9 109-75-1 131-17-9 1838-59-1 2408-20-0 16770-74-4 31001-65-7
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, mercapturic acid formation in)

L30 ANSWER 37 OF 38 CA COPYRIGHT 2002 ACS
AN 76:107812 CA Full-text
TI Alkylating esters. IV. Metabolism of propane-1,3-dimethanesulfonate and its relevance to the mode of action of myleran
AU Edwards, K.; Jones, A. R.
CS Paterson Lab., Christe Hosp., Manchester, Engl.
SO Biochem. Pharmacol. (1971), 20(8), 1781-6
CODEN: BCPCA6
DT Journal
LA English
CC 1 (Pharmacodynamics)
AB Both rats and mice given labeled propane-1,3-dimethanesulfonate (I) [15886-84-7] i.p. excreted unchanged I together with methanesulfonic acid [75-75-2] and S-(3-hydroxypropyl)cysteine N-acetate [**23127-40-4**]. Rats also excreted S-(3-hydroxypropyl)cysteine [13189-98-5], and mice excreted propane-1,3-diol [504-63-2]. Both I and its homolog, Myleran [55-98-1], have comparable distributions in mouse tissues and share similar antispermatogenic and hemopoietic activities in rodents. Sulfur stripping reactions did not occur in vitro or in vivo with I, yet its distribution and pharmacol. effects closely resembled those of Myleran, suggesting that such reactions may not be important to the biol. activity of either compound
ST propanedimethanesulfonate metab; methanesulfonoxyalkane diester
IT 55-98-1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cytotoxic activity of, propanedimethanesulfonate in relation to)
IT 75-75-2 504-63-2 13189-98-5 **23127-40-4**
RL: FORM (Formation, nonpreparative)
(formation of, as propanedimethanesulfonate metabolite)
IT 15886-84-7
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism and cytotoxic activity of, Myleran in relation to)

L30 ANSWER 38 OF 38 CA COPYRIGHT 2002 ACS
AN 74:40109 CA Full-text
TI Mercapturic acid formation from allyl compounds in the rat
AU Kaye, C. M.; Young, Leslie
CS Dep. Biochem., St. Thomas's Hosp. Med. Sch., London, Engl.
SO Biochem. J. (1970), 119(5), 53P
CODEN: BIJOAK
DT Journal
LA English
CC 11 (Mammalian Biochemistry)
AB Allylmercapturic acid was isolated from the urine of rats dosed with S-allyl-L-cysteine, allyl bromide, allyl iodide, triallyl phosphate, or Na allyl sulfate. Crotylmercapturic acid was found in the urine of rats injected with crotyl chloride. 3-Hydroxypropylmercapturic acid was isolated as dicyclohexyl-ammonium salt from the urine of rats dosed with allyl alc.
ST allyl compds metab; mercapturic acids allyl crotyl; crotyl mercapturic acids
IT Urine
(mercapturic acids of, after allyl compound administration)
IT 106-95-6 556-56-9 591-97-9 1623-19-4 19037-59-3 21593-77-1
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metabolism of, mercapturic acid formation in)
IT **23127-19-7**
RL: BIOL (Biological study)
(of urine, after allyl alc. administration)
IT 23127-20-0
RL: BIOL (Biological study)
(of urine, after allyl compound administration)
IT 32155-96-7
RL: BIOL (Biological study)
(of urine, after crotyl chloride administration)